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HYPOFIBRINOGENAEMIA

WITH SPECIAL REFERENCE TO SEVERE CONCEALED ACCIDENTAL HAEMORRHAGE

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One of the few major advances in the practice of obstetrics in the last decade has been the discovery of coagulation defects in pregnancy associated mainly with a reduction or lack of fibrinogen in the plasma.

As long ago as 1769 Morgani noticed that blood sometimes failed to clot at necropsy, and Hunter in 1794 observed that blood was deprived of its powers of coagulation in cases of sudden death. Early in the present century Blair Bell[1] found that menstrual blood contained neither fibrin ferment nor fibrinogen, but it was only in 1936 that Dieckmann[2] first indicated the true nature of the coagulation defect in association with abruptio placentae. Since then a similar coagulation defect has been described in many different circumstances.

In obstetric practice this hypofibrinogenaemia is most commonly associated with severe forms of accidental haemorrhage, less commonly following an intra-uterine foetal death of some standing, and rarely with amniotic-fluid embolism.

It has also been described following incompatible blood transfusions,[3] and ruptured uterus.[4] Recently Beischer[5] has described the condition occurring after apparently normal deliveries, and Winch and Bryans[6] have described one case associated with a retained intra-abdominal placenta after removal of an extra-uterine pregnancy.

Whilst it is not the purpose of this paper to discuss the exact mechanisms of the mode of production of this hypofibrinogenaemia, it is worth mentioning that three main theories exist, of which none is entirely satisfactory:

1. A thromboplastin theory, where it is postulated that thromboplastins are absorbed from the liquor amnii and uterine tissues, causing a widespread deposition of fibrin emboli in the vascular bed.

2. A fibrinolysin theory, which postulates the release of fibrinolysins from a damaged uterine muscle which inactivate or dissolve the available circulating fibrinogen.

3. A theory in which it is thought that a large portion of the available fibrinogen is used up at the site of the retroplacental clot, with perhaps a subsequent release of fibrinolysins.

THE PRESENT INVESTIGATION

70 patients with severe accidental haemorrhage (abruptio placentae) were found among 26,478 patients delivered in the Obstetric Unit of the University of Natal at King Edward VIII Hospital between 1 January 1958 and 31 December 1959. Only severe cases of accidental haemorrhage, where there was evidence of shock, intra-uterine death, and acute abdominal tenderness, were included.

Discussion of the Findings

The incidence of severe accidental haemorrhage was higher than described elsewhere in the literature, being no less than 0·3%. Similarly, the incidence of a serious clotting defect among the 70 patients in this series was high, being 62% (43 cases).

Naturally, the incidence of hypofibrinogenaemia associated with accidental haemorrhage will vary according to the criteria used in its diagnosis. Thus Barry *et al.*[7] in Dublin stated that 'the clotting defect is to be found in the majority of, if not all, cases of combined and concealed haemorrhages', whereas Beischer[5] found a clotting defect in 3·5% of patients with accidental haemorrhages, and Porter[3] an incidence of 42%.

Of our 46 cases of hypofibrinogenaemia, 44 were associated with abruptio placentae. One was associated with an intra-uterine death at 30-weeks period of gestation, and 1 was associated with a ruptured uterus which developed after a Caesarean hysterectomy had been performed. The incidence of hypofibrinogenaemia per total deliveries was 0·18%, which is 18 times higher than that found by Scott[8] in Liverpool.

Increasing parity appeared to predispose to hypofibrinogenaemia, for there were only 8·9% (4) primigravid, 63% (29) para 1 - 4, and as many as 28·2% (13) grande multiparous (5 or more pregnancies) patients in the present series, whereas the incidence of primiparae, multiparae and grande multiparae in the general run of deliveries was 29%, 56%, and 17% respectively.

Although it is traditional to associate hypertension or pre-eclampsia with abruptio placentae, the association is often impossible to establish in the presence of shock, and in many of our patients the hypertension did not become manifest until after resuscitation of the patient. Eastman[10] is of the opinion that 'with each passing hour abruptio conduces more and more to hypertension and albuminuria'.

It is not surprising, therefore, that the incidence of toxaemia in abruptio placentae is uncertain — being reported for instance by Kimbrough[11] as 8%, and as 66% by Adams.[12] In the present series definite evidence of hypertension with or without superimposed toxaemia was found in but 29% (13 cases), which contributes little to solve 'which is the horse and which is the wagon'.

Barry[7] has suggested that malnutrition and anaemia are important associated factors, and Kwaan *et al.*[13] have shown that an increased fibrolytic activity is associated with cirrhosis of the liver. Certainly in our patients hypoproteinaemia, an inverted albumin/globulin ratio, and

minor liver dysfunction are 'normal' findings, malnutrition being rife; but anaemia *per se* is comparatively rare in the African.

However, their fibrinogen levels are normal and their fibrinolytic activity is lowered during pregnancy.[14] The effect of this liver dysfunction on the clotting mechanism is at present undergoing investigation. These factors may possibly explain the relative frequency of hypofibrinogenaemia in our practice.

An important point lies in the previous history of accidental haemorrhage. Porter[8] found the incidence of abruptio placentae in a subsequent pregnancy was as high as 12% and Fyfe and Grant[15] describe a case of afibrinogenaemia in two successive pregnancies. Only one of our patients had a history of having had a previous antepartum haemorrhage.

A further important consideration is a history of a small antepartum haemorrhage at an earlier stage of the pregnancy. Two of our patients had been discharged following investigation for a small antepartum haemorrhage after placentography had demonstrated a normally situated placenta, only to be readmitted later, having had a severe accidental haemorrhage.

The Diagnosis of Hypofibrinogenaemia

The first prerequisite in the diagnosis of hypofibrinogenaemia is to be aware of its existence and suspect its presence in all patients with severe accidental haemorrhage and all patients with a bleeding tendency, either in pregnancy or immediately after delivery. Even then there may be a considerable delay in diagnosis.

Numerous qualitative and quantitative tests have been described in the investigation of the bleeding tendency. We have found Weiner's clot-observation test the most useful, and this is carried out as a routine in every patient with antepartum haemorrhage. This test has the advantage of simplicity and rapidity. However, Sharp *et al.*[16] consider that tests based on the reactivity of plasma to purified thrombin are the most reliable.

In every patient where a clinical possibility of a clotting defect existed or was suspected on the clot-observation test, a routine quantitative estimation of the fibrinogen level was performed, using the method described by Stirland in 1956.[17] Where doubt remained reliance was primarily placed on the bedside tests. A modified Schneider test was also performed in equivocal cases. These tests were repeated hourly, as necessary, during the treatment of the patient. Where error in diagnosis occurred, it resulted from failing to perform the tests rather than from any inaccuracy in the results.

Tests for a heparin-like factor and circulating fibrinolysins (other than the clot-observation test) have not been performed as a routine up to the present.

Treatment

The treatment of hypofibrinogenaemia varies greatly from centre to centre. We have found the following routine to give the most satisfactory results:

In the vast majority of patients with severe accidental haemorrhages of sudden onset we have found that there are at least 2-3 pints of retroplacental blood clot. We believe, therefore, that 2-3 pints of blood can be transfused rapidly in these cases with safety, to restore the blood volume and thus prevent the danger of renal arteriolar spasm with subsequent renal damage. Calcium gluconate is given with the blood as required, to counteract possible citrate effects.

The slow pulse often found, even in patients with severe accidental haemorrhage, tends to give the unwary a false sense of security, whereas these patients should nevertheless be treated along the routine lines. If hypovolaemia is not corrected, then a further small haemorrhage may easily precipitate a state of profound shock.

Additional defects in other sections of the clotting mechanism may also assume dominant rôles in recalcitrant cases, and 'fresh' blood, while not containing more fibrinogen than stored blood, may be beneficial.

At the same time as the blood volume is being restored, fibrinogen is replaced as required, either in the form of triple-strength plasma containing about 3 G. per unit, or as purified human fibrinogen. Of the two, our recent preference is for the purified fibrinogen since it requires less volume, weight for weight, and the fibrinogen content is more accurately known. Jeffcoate and Scott[18] have suggested that plasma may be more effective than fibrinogen. However, this has not been our experience; indeed, we are opposed to it since we have observed a tendency to hypervolaemia and subsequent pulmonary oedema with its use.

The hypovolaemia and the clotting defect should be corrected simultaneously, lest by raising the blood pressure without controlling the coagulation defect, further and possibly fatal haemorrhage may be precipitated.

We have found that certain patients require very large amounts of fibrinogen to restore the clotting mechanism to normal. In such patients intravenous cortisone may be helpful, according to Moore,[8] in order to speed the combination of plasmin (fibrinolysin) with an anti-plasmin, thus reducing fibrinolytic activity which may be increased in the presence of profound shock.

Our experience agrees with the leading article in the *British Medical Journal*[19] that defibrination is usually 'a once for all mechanism', but if the interval between the onset of haemorrhage and the delivery becomes prolonged, particularly in African patients, a recurrence of the clotting defect often occurs.

We have never found any evidence of an intravascular fibrin deposition of sufficient magnitude to produce any signs either during the delivery or in the puerperium, and so have not considered the use of heparin.

The amount of fibrinogen used depends on the progress of the clotting defect. Barnett and Cussen[20] have found very small doses of fibrinogen to be effective in some patients, but others give 4-8 G. empirically. We have found anything less than an initial dose of 3 G. inadequate in the type of patient under consideration.

Once the hypovolaemia and clotting defect have been corrected, then, and only then, is an effort made to expedite delivery, which is done by artificially rupturing the membranes. Immediate rupture of the membranes, as advocated by some authorities, is dangerous in serious cases.

If, one hour after rupture of the membranes, the patient shows no signs of going into labour, despite the presence of a cervix which is not too unfavourable, a pitocin infu-

sion of 1 part in 2,500 is given to stimulate labour. In the majority of patients these measures result in a rapid onset of labour. If, after 4 hours on a pitocin drip, labour is not well established and making good progress, the pregnancy is usually terminated by lower-segment Caesarean section, after again checking that the blood defect has remained corrected.

There are of course dangers in the use of pitocin and cases of high multiparity should be excluded. The theoretical danger of increasing the incidence of anuria has not been borne out in our series.

Obstetrical complications, such as malpresentation and cephalopelvic disproportion, are treated on their merits with early recourse to Caesarean section if there are signs of a difficult delivery ahead. Caesarean section is also performed in patients where there is evidence of a recurrence of the clotting defect, after again correcting this defect.

The one patient in whom intra-uterine death was associated with hypofibrinogenaemia was treated conservatively in this series by awaiting the spontaneous onset of labour and then rapidly correcting the coagulation defect. If, however, the bleeding tendency causes serious symptoms, then there may be a place for Caesarean section after correction of the clotting defect.

One of the practical difficulties in the management of these patients is the correlation of the clinical state, the serial investigations, and the progress being made, with the treatment given. To facilitate the management of these patients we have modified the 'flow sheet' (Caillouette *et al.*[21]) so that all necessary information is readily available.

The results obtained in the treatment of 45 patients with hypofibrinogenaemia associated with abruptio placentae are shown in Table I.

TABLE I. RESULTS OF TREATMENT

Vaginal Deliveries; Total 34	
(*i*) Without pitocin drip	24
(*ii*) With pitocin drip	9
(*iii*) With pitocin drip and low forceps extraction	1
Lower-segment Caesarean Section; Total 10	
(*i*) For obstetrical causes	5
(ii) For failure to respond to treatment	5
Caesarean Hysterectomy; Total 1	

The foetal mortality was 100% and 1 maternal death occurred in this series. This occurred in a para 3 aged 28 years, who sustained a ruptured uterus during the delivery of a hydrocephalic infant. The clotting defect appeared late in treatment after the Caesarean hysterectomy had been performed. She was given 18 pints of blood and 15 G. of fibrinogen before she died. At post-mortem examination the cause of death was found to be a slipped ligature on the uterine artery.

Two patients developed acute pulmonary oedema during treatment. This was ascribed in both to the excessive use of triple-strength plasma. Both patients responded to digitalization and venesection.

The complication of postpartum haemorrhage arose in 6 patients. In 4 of these, treatment of the clotting defect was inadequate, and in the other two insufficient time elapsed between admission and delivery for completion of adequate treatment.

Only in one patient severe oliguria occurred in association with hypofibrinogenaemia. It occurred in a hypertensive para 6, aged 26, who was admitted with revealed and concealed accidental haemorrhage, which had occurred 3 hours before admission. Her blood pressure was 170/120 mm.Hg on admission. Her lowest urinary output in 24 hours was 150 ml. and the highest blood-urea recording was 280 mg. per 100 ml. on the 9th day after delivery. She responded well to treatment and was discharged.

Until a few years ago severe accidental haemorrhage had always been associated with a high maternal mortality in which acute renal failure played a large part. In 1950, for instance, one of us (D.C., 1950[22]) found an anuria rate of 11·6% and a maternal mortality rate of 10·9% in a large series of patients treated at the Peninsula Maternity Hospital, Cape Town.

In the present series the single maternal death was mainly caused by factors other than the hypofibrinogenaemia, and the only case of observed oliguria occurred where there was probably already some predisposing renal arteriolar spasm with the hypertension associated with unpreventable delay in the onset of treatment.

We ascribe these results to 3 main principles of management: Firstly, the rapid correction of the hypovolaemia with blood; secondly, the rapid correction of the hypofibrinogenaemia with adequate quantities of fibrinogen as indicated by the clot-observation test and quantitative fibrinogen estimation; and finally, refraining from expediting vaginal delivery until the situation is well controlled, with Caesarean section occupying an important place in the treatment of patients with the complication of an unfavourable cervix, recurrence of hypofibrinogenaemia or shock, or a delayed onset of haemorrhage-delivery interval.

SUMMARY

1. A study of 46 patients with serious hypofibrinogenaemia is presented occurring among African and Indian patients. Of these 44 were associated with severe concealed accidental haemorrhage.

2. The frequency of liver dysfunction among the Africans was considered a possible aetiological factor in the high incidence of hypofibrinogenaemia found in accidental haemorrhage (62%) and among the total deliveries (0·18%). Grande multiparity was also found to predispose to hypofibrinogenaemia.

3. Both the hypovolaemia and the clotting defects were found to be complications in accidental haemorrhage which required correction as emergency measures — preferably within an hour of the admission of the patient. The use of fibrinogen was found to be preferable to that of triple-strength plasma in such circumstances.

4. Defibrinogenation is not always a 'once for all mechanism', and the most serious cases are prone to develop a recurrence of hypofibrinogenaemia following the initial correction (particularly among our African patients). Consequently Caesarean section plays an important rôle in the treatment of severe cases associated with a prolonged interval between the onset of accidental haemorrhage and the anticipated vaginal delivery.

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REFERENCES

1. Bell, W. Blair (1911): Proc. Roy. Soc. Med., **4,** 234.
2. Dieckmann, W. J. (1936): Amer. J. Obstet. Gynec., **31,** 734.
3. Moore, J. M. (1958): Brit. Med. J., **2,** 1201.
4. Riedel, J. A. (1958): J. Obstet. Gynaec. Brit. Emp., **65,** 652.
5. Beischer, N. A. (1959): Med. J. Aust., **2,** 180.
6. Winch, G. C. and Bryans, F. E. (1960): J. Obstet. Gynaec. Brit. Emp., **67,** 646.
7. Barry, A. P., Geoghegan, F. and Shea, S. M. (1955): Brit. Med. J., **2,** 287.
8. Porter, J. (1960): Obstet. and Gynec., **15,** 690.
9. Scott, J. S. (1955): Brit. Med. J., **2,** 290.
10. Eastman, N. J. (1960): Obstet. and Gynec., **15,** 199.
11. Kimbrough, R. A. (1959): Amer. J. Obstet. Gynec., **78,** 1161.
12. Adams, J. Q., Henry, L. C. and Schreier, P. C. (1959): Obstet. and Gynec., **14,** 724.
13. Kwaan, H. C., McFadzean, A. J. and Cook, J. (1956): Lancet, **1,** 132.
14. Gillman, T., Naidoo, S. S. and Hathorn, M. (1959): *Ibid.*, **2,** 70.
15. Fyfe, A. E. and Grant, M. (1960): J. Obstet. Gynaec. Brit. Emp., **67,** 649.
16. Sharp, A. A., Howie, B., Biggs, R. and Methuen, D. T. (1958): Lancet, **2,** 1309.
17. Stirland, R. M. (1956): Lancet, **1,** 672.
18. Jeffcoate, T. and Scott, J. (1959): *Ibid.*, **1,** 313.
19. Leading Article (1960): Brit. Med. J., **1,** 789.
20. Barnett, V. H. and Cussen, C. A. (1954): *Ibid.*, **2,** 676.
21. Caillouette, J. C., Longo, L. D. and Russell, K. P. (1959): J. Amer. Med. Assoc., **170,** 1520
22. Crichton, D. (1950): Brit. Med. J., **1,** 401.

BIBLIOGRAPHY

Barry, A. P., Feeny, J. and Geoghegan, F. (1955): Brit. Med. J., **2,** 12.
Friedman, S. and Anderson, G. D. (1958): N.Y. St. J. Med., **58,** 4077.
Holmes, J. M. and Eyears, L. W. (1957): J. Obstet. Gynaec. Brit. Emp., **64,** 903.
Jennison, R. F. and Walker, A. H. C. (1956): Lancet, **2,** 607.
Kimbell, N. and Gosh, A. K. (1956): *Ibid.*, **2,** 80.
MacGregor, W. G. and Tovey, A. D. (1957): Brit. Med. J., **2,** 855.
Mole, R. H. (1948): J. Path. Bact., **60,** 413.
Pritchard, J. A. and Ratnoff, O. D. (1955): Surg. Gynec. Obstet., **101,** 467.
Reid, D. E., Weiner, A. E. and Roby, C. C. (1953): Amer. J. Obstet. Gynec., **66,** 465.
Idem (1953): *Ibid.*, **66,** 500.
Schneider, C. L. (1947): Amer. J. Physiol., **149,** 123.
Idem (1952): Amer. J. Obstet. Gynec., **64,** 141.
Weiner, A. E., Reid, D. E. and Roby, C. C. (1953): *Ibid.*, **66,** 475.
Idem (1950): *Ibid.*, **60,** 379.

SALMONELLA BELLVILLE

'N VERDERE NUWE SEROTIPE (16 : e,n,x : 1,7)

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Op 8 Julie 1960 het ons van een en dieselfde stoelgangmonster, wat van 'n Blanke 10-jarige kind met koorsigheid, braking, maagpyn, en 'n matige geelsug verkry is, tegelykertyd 'n patogene *E. koli* tipe O 119 en 'n salmonella gekweek. Onder kliniese behandeling het die pasiënt vinnig verbeter.

Hierdie salmonella was nie teenwoordig in die Kauffmann-White skema nie. Die biochemiese reaksies was soos volg: ureum, indol, KCN, laktose, saccharose, raffinose, inosiet, eskulien, adoniet, en salisilaat: negatief. Daar was suur- en gas-formasie in dekstrose, manniet, dulsiet en sorbiet; slegs suur, maar geen gas nie, in eksilol; en H_2S-formasie was sterk positief. Alle positiewe reaksies was binne 48 uur sigbaar.

Serologies het agglutinasie plaasgevind met die O-agglutinien 16 en met die sweephaaragglutiniene e, n, en x, sodat ons primêr aan 'n tweede onspesifieke fase gedink het, want die e,n,x-kombinasie is meestal kenmerkend daarvan. Vir verdere bestudering is hierdie stam na die Salmonella-sentrum in Londen gestuur en ondersoeke is ook in Chamblee, Georgia (V.S.A.), en in Kopenhagen gedoen. Die definitiewe seroformule is as 16 : e,n,x : 1,7 bepaal. Aangesien die pasiënt in die omgewing van ons hospitaal woonagtig is, het ons vir die nuwe salmonella die naam *S. bellville* voorgestel. Intussen is hierdie naam internasionaal aanvaar. *S. bellville* is een van die skaars tipes wat die e,n,x-kompleks as eerste spesifieke H-fase het. (Tot nog toe is daar slegs *een* ander salmonella met e,n,x in die spesifieke fase, nl. *S. lindrick*.)

S. bellville was primêr weerstandig teenoor penisillien, eritromisien en novobiosien, maar gevoelig vir streptomisien, chloramfenikol, kanamisien, en alle tetrasiklienes.

Salmonella bellville, A FURTHER NEW SEROTYPE (16 : e,n,x : 1,7)

This new salmonella was isolated from faeces of a 10-year-old European boy from the neighbourhood of our hospital. Simultaneously a pathogenic *E. coli* type O 119 was obtained. Two months before hospitalization the patient's faeces contained blood. On admission fever was present, together with vomiting, stomach cramps, and moderate jaundice. The patient recovered quickly after a few days of clinical treatment.

The following biochemical properties were determined: urea, indol, KCN, lactose, saccharose, raffinose, inositol, aesculin, adonit, and salicin: negative. There was acid and gas formation in dextrose, mannitol, dulcitol and sorbitol; only acid formation in xylose; and H_2S-production was stormy. Gelatine was liquefied after 32 days.

On serological examination *S. bellville* was agglutinated by the O-antiserum 16 and by the agglutinins e,n and x. Therefore we thought the strain would be in the second phase and posted it to the Salmonella Reference Laboratory, London, for further observations. Meanwhile the definite sero-formula was determined as: 16 : e,n,x : 1,7. The name *S. bellville* has been accepted internationally.

S. bellville was found to be primarily resistant to penicillin, erythromycin and novobiocin, and sensitive to streptomycin, chloramphenicol, kanamycin, neomycin, and all the tetracyclines.

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VAN DIE REDAKSIE : EDITORIAL

DIE VERVOER VAN BESEERDE PASIËNTE

Een van die groot moeilikhede by die behandeling en bevredigende hantering van ernstig beseerde pasiënte, is die groot afstand tussen hospitale. Alhoewel ons paaie, wat van jaar tot jaar verbeter, tot ons skat van skoonhede in die land behoort, vorm hulle ook 'n bron van groot bekommernis aangesien jaarliks meer en meer padongelukke voorkom— 'n toestand van sake wat saamhang met die verbeterde padoppervlaktes en die kragtiger motors wat in steeds groter getalle beskikbaar word. 'n Motorongeluk in die stad is ernstig genoeg — op die platteland is trouma as gevolg van jaery dikwels noodlottig. Dit is bekend dat ongelukke op die platteland dikwels ernstiger is as in die stede — 'n toestand van sake wat weerspieël word in die groter sterftesyfer na ongelukke: 2% in stedelike gebiede teenoor 12% onder vergelykbare omstandighede op die platteland.

Die sleutel tot goeie behandeling van beseerdes lê ongetwyfeld in goeie vervoerreëlings. Daar is ooreenstemming by militêre en siviele outoriteite dat, as alles in ag geneem word, beter resultate met behandeling van beseerdes verwag kan word as die beseerde persoon so gou as moontlik vervoer word sodat hy bevredigende mediese en verplegingsbehandeling kan ontvang. Die daaropvolgende ongeskiktheidsperiode kan ook hierdeur verkort word. Selfs goeie vervoer en versigtige hantering kan egter nie voorkom dat bykomstige besering ontstaan nie. Dit is dus noodsaaklik dat daar versigtig besluit moet word oor die relatiewe voor- en nadele van onmiddellike vervoer of opwekking op die plek van die ongeluk.

Dit is hier — by die vroeë en noodsaaklike opsomming van die geval — dat die geneesheer toon wat hy beteken. Die medisyne bly nog 'n kuns, en dit is by hierdie belangrike besluite dat opleiding en ondervinding die meeste tel. Alhoewel die besluit gou geneem moet word, laat goeie eerstehulp-maatreëls tog ruimte vir speling. As die essensiële voorwaardes van 'n oop lugweg en beheer van bloeding dus nagekom is, kan daar 'n verposinkie wees waarin om te besluit of dit in die beste belange van die pasiënt sal wees om hom dadelik te vervoer of nie. Daar is nie baie maatreëls wat as roetine vir alle gevalle toegepas kan word nie — as dit anders was, sou behandeling deur persone sonder spesiale opleiding onderneem kon word. Die groot verskeidenheid van omstandighede by elke ongeluk en die individuele variasies sal nog lank voorkom dat ons robot-praktyke in hierdie gevalle toepas.

Sodra die besluit geneem is om die pasiënt te vervoer, moet die ‚gladste' metode gebruik word. Oor kort afstande van 'n paar myl of so is die gewone motorambulanse heeltemal doeltreffend. As die afstande egter groter as 30 of 40 myl is, tree die nadelige gevolge van dié soort vervoer te voorskyn, en die bloeddruk van die pasiënt daal na gelang sy toestand van skok vererger. Terwyl ons dus skaars iets beters kan bedink as motorvervoer in die stede en omstreke, moet ons spesiale aandag skenk aan die verbetering van vervoerdienste op die platteland.

Miskien sou vervoerdienste oor afstande van 30 - 100 myl op die beste manier gereël kon word deur gebruik te maak van helikopters — indien so 'n diens beskikbaar gestel sou kon word. Die beseerde kan dan na die naaste hospitaal vervoer word waar opwekking en behandeling onderneem kan word op die grondslag van bestaande en aanvaarde beginsels.

Wat met die pasiënt gebeur nadat hy na 'n hospitaal toe vervoer is, hang in 'n groot mate van regeringsbeleid af. Tot onlangs is dit aangeneem dat alle hospitale ewe goed toegerus is om mediese en verplegingsdienste te lewer aan beseerdes. Daar word nou egter al meer besef dat alle hospitale nie ewe goed in hierdie behoefte kan voorsien nie. Spesiale afdelings moet beskikbaar gestel word (asook spesiale fasiliteite) om gevalle van veelvoudige besering op die beste manier te kan hanteer. Dit is juis hierdie soort gevalle wat so baie bekommernis vir die dokter en so veel ellende en ongeskiktheid vir die pasiënt veroorsaak.

Aangesien trouma hom nie steur aan die kunsmatige indeling van ons verskillende spesialiteits-rigtings nie, mag dit wel by geleentheid op kort kennisgewing nodig wees om gebruik te maak van al die bronne van 'n goed-toegeruste hospitaal. Dit mag selfs nodig wees om sekere gevalle, nadat opwekking en voorlopige behandeling in die naaste hospitaal uitgevoer is, na een van 'n halfdosyn of meer spesiale ongevalle-hospitale oor te plaas. Eenhede soos hierdie moet by voorkeur verbonde wees aan goedtoegeruste opleidingshospitale.[1]

Vir hierdie soort vervoer, nl. van verafgeleë hospitale af na spesiale ongevalle-hospitale toe (op die grondslag van die groot afstande in ons land) moet ligte lugskepe gebruik word. Vervoer kan dan veilig, en sonder veel verdere trouma en verlies van tyd, behartig word.

Die ambulans- en transportdienste wat ons hier in die vooruitsig gestel het, mag wel baie duur kos en dus nie binne die grense van die uitvoerbare val nie. Dienste van hierdie aard sou egter teen 'n redelike onkoste onderneem kon word indien bevredigende skakelreëlings bestaan tussen ambulansdienste en die lugdienste. Dit sou miskien moontlik kon wees om ligte lugskepe en helikopters gereed te hou by die bestaande vliegvelde wat orals oor die land versprei is. Hulle kan dan beskikbaar wees indien nodig, en hulle hoef dan nie as bykomstige las op die ambulansdienste as sodanig te rus nie. Ons lugdienste word op 'n hoë vlak van doeltreffendheid beheer, en bykomstige pligte soos die wat ons geskets het, sou kon bydra om die waarde en betekenis van die lugdienste van ons land te verhoog.

Dit lyk of die tyd aangebreek het vir die mediese professie om by die regering aan te dring daarop om by te

dra tot die skepping van bevredigende ambulansdienste vir alle beseerdes. Die aantal padongelukke en sterftes as gevolg van ongelukke vermeerder elke week. Dit sou ons hande oneindig sterk as 'n woordjie, wat op die regte plek gespreek word, kon help om doeltreffende mediese dienste op die vroegste moontlike tyd beskikbaar te stel. Dit is 'n saak wat ons nie langer durf uitstel nie.

1. Aantekening (1961): Lancet, **2**, 141.

TRANSPORTING THE INJURED

One of the difficulties in treating and salvaging patients who have been involved in serious accidents in this country, arises from the great distances that exist between hospitals. On our network of great country roads (one of the unpublicized wonders of Africa), the speed of vehicles increases year by year as road surfaces are improved and with more powerful car engines becoming more readily available to the general public. A motor accident in the towns is bad enough — in the country districts at high speeds the trauma is appalling. Consequently, injuries in the country tend to be far more severe than in similar accidents in the towns, and this is reflected in the mortality rate: 2% in town motor accidents as opposed to 12% in similar circumstances in the country.

Good transport of the injured is undoubtedly the key to better results in treatment. Military as well as civil authorities concerned with the treatment of accidents agree that, all things being equal, the sooner an injured person is removed to proper nursing and medical care, the better will be the results of treatment and the less prolonged will be the period of disability which is inevitable after any injury. However good transport may be, a certain amount of pain and additional injury is inflicted even by gently moving a person already injured, so that a very careful assessment of the relative value of early transport must be made immediately, and its advantages must be weighed against those of resuscitation on the spot.

It is in this early and essential assessment that the worth of the medical man declares itself. Medicine is still an art, and it is in these crucial decisions that experience and training count most. The decision may well have to be made rapidly, but proper first aid will allow a little latitude in these matters so that, if the basic requirements of an open airway and control of haemorrhage are achieved, some short time may be spent in deciding whether the interests of the patient are best served by moving him or not. There are very few therapeutic manoeuvres that can be applied without question to all cases. If this were not so, much therapy could be prescribed by rule of thumb, and the practice of medicine could be undertaken by non-registered robots. The variations in the conditions of the patients and in the individual circumstances of each injury make it quite certain that we shall have to wait a long time before the age of robot medicine is upon us.

Once it has been decided to move the patient, the smoothest, easiest and least-jolting method must be employed. For short runs of a few miles, the ordinary motor ambulance serves very well, but after 30 or 40 miles the noxious effects of transport, even in this type of ambulance, become apparent and the blood pressure of the patient drops as his state of shock increases. While, therefore, we cannot do better than to use motor transport in the towns and their near vicinity, attention should be directed to improving services further outside the towns themselves.

The improvement in transport services for these relatively short hauls (30 - 100 miles) could perhaps best be achieved in country districts and in districts close to the towns by making available helicopter services to fetch the injured from the scene of a road accident to the nearest hospital where adequate resuscitation methods can be employed according to those simple basic principles that have long been known and practised.

What happens to the patient after he is moved to the hospital is going to depend on government policy. Until recently all hospitals were considered equally capable of handling all cases of trauma, and the patients were treated to the best ability of the medical and nursing staff of the hospital concerned. But it is now becoming recognized that all hospitals are not equally efficient in dealing with all cases of trauma. Special wards have been set aside or special hospitals have been built with special facilities to deal with accidents, particularly with those difficult cases of multiple injuries and serious accidents that cause so much worry to the doctor and so much misery and disability to the patient. Since trauma knows no anatomical bounds and does not respect the artificial boundaries of our registrable specialties, the whole resources of even a well-equipped hospital may be called upon at short notice to deal with these patients. It may be advisable to transfer these 'special' patients, once resuscitation in the nearest hospital has been achieved, to one of a half dozen special accident centres which it is now generally agreed can only exist within or close to a teaching hospital.[2]

For this type of transport, i.e. from the outlying hospital to the accident centre, taking the size of our country and the long distances involved into consideration, light aircraft should be employed. Transport can then be effected safely, with no additional unnecessary trauma and with a negligible loss of time.

The ambulance and transport service which we have envisaged may well be found to be very expensive and, as such, Utopian and impossible of fulfilment. However, this apparently very expensive service can be provided at a reasonable cost to the country if proper liaison can be achieved between the ambulance services and the airforce. It may well be possible to maintain light aircraft and helicopters in the ordinary airforce aerodromes, which are dotted all over the country, so that they should be available when necessary; and their maintenance need not fall as an additional charge entirely on to the ambulance services themselves. The airforce is being maintained at a high level of efficiency by the authorities, and this additional duty would serve the double purpose of justifying its existence and of keeping the crews and material at a proper level of preparedness.

It is time that the profession came out with a statement

urging the government to undertake to improve the ambulance services available to all injured. The number of road casualties and fatalities increases from week to week. We can ill afford to lose these people if a word in the right quarter can help us to bring them under more efficient medical care in less time. The matter is urgent.

1. Annotation (1961): Lancet, **2**, 141.

THE ELLISON-ZOLLINGER SYNDROME AND HYPERPARATHYROIDISM IN RECURRENT PEPTIC ULCERATION

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The occurrence of hyperparathyroidism does not often warrant its publication. However, the growing realization that recurrent peptic ulceration is not uncommonly associated with endocrine imbalance is the reason for this timely reminder. The unabated and relentless progress of ulceration in the upper gastro-intestinal tract has been, in recent years, tied up with non-insulin secretory tumours of the islet cells of the pancreas (α, γ, and Δ cells). The recent literature abounds with reports of the so-called Ellison-Zollinger syndrome;[1] they all stress the importance of multiple endocrine dysfunction. When we attempted to prove that our case was an example of this syndrome, this knowledge of endocrine interdependence was helpful and led to the diagnosis of a parathyroid adenoma.

CASE REPORT

Mrs. A. G., aged 37, first presented in November 1956 complaining of epigastric pain of 6 weeks' duration. The pain was related to meals and relieved by alkalis. She was often awakened by the pain at night, which was only partially relieved by the usual medication and diet. Vomiting occurred after meals and relieved the pain. Loss of weight had been quite marked. Examination revealed no obvious cause and a barium meal showed a duodenal ulcer. She was treated as an inpatient for 6 weeks without improvement. She continued on an ulcer régime and was first seen at this hospital in February 1957. Her symptoms and signs were of such severity that she was admitted with the diagnosis of pancreatitis.

A barium meal confirmed the presence of a duodenal ulcer, and she remained in hospital for 1 month on strict medical treatment. Her poor progress is shown by the fact that within 3 days of discharge she was re-admitted with the diagnosis of an acute flare-up of a peptic ulcer. A barium meal on this occasion (1 month after the previous X-ray) showed no change in the duodenal deformity. Gastric analysis showed a hydrochloric-acid level of 70 mEq. per litre (normal 20 - 50 mEq. per litre). The pH was not recorded. A decision was made to operate because of the lack of response to medical treatment. In April 1957 a laparotomy confirmed the presence of a penetrating duodenal ulcer and an ante-colic Polya gastrectomy was performed. Her convalescence was smooth and she was discharged from hospital fairly well 3 weeks after operation. The patient progressed favourably until November 1957, at which time she had vague abdominal pains after meals and occasionally at night, which were relieved by milk and alkalis. The pains continued irregularly until their intensity increased in December 1957 and she was re-admitted for emergency treatment. The severity of the pain and the physical features were such that a perforated anastomotic ulcer was diagnosed, and at laparotomy this was confirmed and sutured. She made a satisfactory recovery and before discharge a gastric analysis showed a hydrochloric-acid level of 40 mEq. per litre.

Soon after the operation she again experienced abdominal discomfort after meals, and excessive flatulence. She was re-admitted in February 1958 for re-assessment. A barium meal on this occasion showed no ulcer or hold-up or evidence of dumping. The blood-urea and urine examinations were normal. From this time until her next admission in December 1958 her story was one of persistent dyspepsia and epigastric discomfort, with considerable loss of weight. It is interesting to note the remark of the intern in his notes of 1958: '. . . she is a thin, wasted and unhappy patient. . . . '. A barium meal failed to reveal any abnormality. Gastric analysis was not significant; urine, blood count and blood urea were all within normal limits.

This patient certainly presented a vexing problem, and it was the general consensus of opinion that an attempt should be made to refashion her gastrectomy, or even to do a higher gastrectomy. At operation, on 4 December 1958, she had a large stomal ulcer penetrating the left lobe of the liver. The previous gastro-enterostomy was undone and a higher gastrectomy, with a new gastro-jejunal anastomosis, was performed. She remained well after this operation, and despite occasional attacks of what she called 'indigestion', she was able to take up her previous occupation as a shop assistant.

In January 1960 she presented with acute colicky pain, acute constipation and vomiting. The symptoms and signs were those of an obstruction. The next day laparotomy revealed adhesions binding the ileo-caecal junction. These were freed, and she made an uneventful recovery. However, from this date until her next admission in June 1960 her progress was one of continued episodes of epigastric pain, vomiting, weakness and gradual deterioration in health. She had lost 60 lb. in weight since 1957. She was finally re-admitted for reassessment on 12 June 1960. A barium meal showed stomal ulceration. Urine, blood, stool, and blood-urea examinations showed no significant change. After 2 weeks in hospital a surgical opinion was requested. The first impression was that, although recurrent ulceration can be most stubborn and resistant to treatment, it is not a common finding in females. It was felt that some other factor or factors could possibly be responsible for the continued ulceration of her upper gastro-intestinal tract. Bearing in mind the relentless nature of her peptic ulceration, we investigated the possibility that this was a case of ulcerogenic tumour of the pancreas. We failed, however, to find any marked gastric hypersecretion, or a very highly acid juice.

Fig. 1. Intravenous pyleogram film showing ectopic foci of calcification in the region of the left kidney.

At the same time we investigated the patient from the point of view of other endocrine imbalance. The glucose-tolerance curve was normal. The blood sugar was normal. The serum calcium was 15·2 mg. per 100 ml. A repeat examination of the serum calcium a few days later showed 14·6 mg. per 100 ml. and the serum phosphorus was 2 mg. per 100 ml. Alkaline phosphatase was 9 King-Armstrong units. A skeletal survey was normal, a carefully controlled urinary calcium-excretion test was within normal limits. An intravenous pyelogram showed normal excretion and no calculi were seen, but the control and intravenous pyelogram films showed ectopic foci of calcification in the region of the kidney on the left side. Screening and A-P views gave the impression that one of the foci was in the left lobe of the liver and the other in the left kidney. The nature of the calcification and the lesion in the kidney suggested a renal cyst with calcification (Fig. 1). The blood urea was normal.

Careful re-examination of the neck enabled us to feel a small swelling in the right thyroid lobe. An X-ray of the chest showed normal lungs and heart and no mediastinal masses. A repeat serum-calcium estimation was 14·4 mg. per 100 ml. and serum phosphorus was 2·6 mg. per 100 ml. The liver-function tests were normal. Serum proteins were 6·8 G. per 100 ml. and the serum albumin/globulin ratio was 1·3 : 1. Phenosulfophthalein and water-concentration tests showed reasonable renal function. It was not felt justifiable to do a 10-day cortisone test, since the diagnosis of primary hyperparathyroidism seemed almost certain. An electrocardiogram showed the typical picture of hypercalcaemia—an almost complete absence of the ST interval (Fig. 2). The diagnosis now seemed certain and was an added stimulus to finding the tumour.

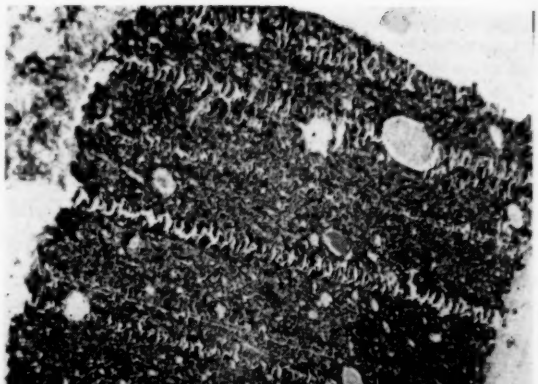

Fig. 3. Microphotograph of parathyroid adenoma removed at operation. It shows uniformity of cell pattern and absence of stomal and adipose tissue. The presence of colloid-like material, as seen in this section, occasionally makes differentiation from thyroid adenomata difficult.

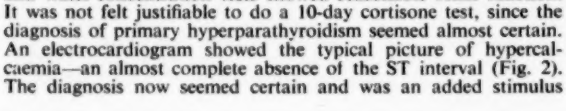

Fig. 2. ECG before operation. Lead II shows typical picture of hypercalcaemia with almost complete absence of the ST interval.

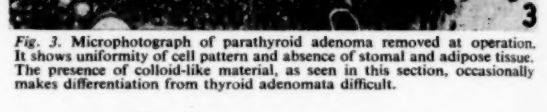

Fig. 4. ECG after operation, with typical prolonged ST segment of hypocalcaemia.

On 2 August 1960 an exploration of the neck was undertaken. Both lobes of the thyroid were fully mobilized. In the left lobe of the thyroid a nodule was palpable in the inferior pole. This nodule was removed. The left superior parathyroid gland was identified and found to be normal, as was the lower parathyroid gland. On the right side at the upper pole postero-medially, attached to, but not completely embedded in, the thyroid was a solid tumour the size of an almond, brownish in colour with an admixture of yellow areas. A superior right parathyroid gland was not seen and the general impression was that this tumour was an adenoma of the right superior parathyroid gland. A right lower parathyroid gland was not identified. Inferiorly, in the suprasternal notch, tissue resembling adipose tissue was dissected and removed. This proved to be normal parathyroid and thymic glandular tissue. The tumour and the right lobe of the thyroid were removed as one block of tissue. Microscopy showed that the left-lobe nodule was a thyroid adenoma and the tumour in relation to the right upper lobe was a parathyroid adenoma (Fig. 3).

Three days after operation the serum calcium was 8·5 mg. per 100 ml., and serial calcium investigations have not shown a figure above 9 mg. per 100 ml. Urinary calcium was 16 mg. per 100 ml. (normal 50 - 300 mg. per 100 ml.). The latest serum-calcium estimation is 7 mg. per 100 ml. There is slight concern that the patient may be going into a state of hypoparathyroidism. At the moment there is no evidence to suggest incipient tetany. Her appetite has improved and she now partakes of a full diet without ill effect.

Recent barium-meal studies show there is no delay in passage of barium through the stoma. No gastric or jejunal ulceration is visible. The patient has put on 10 lb. in weight and is symptom-free.

A recent electrocardiogram has the typical prolonged ST segment of hypocalcaemia (Fig. 4).

DISCUSSION

Ellison-Zollinger Syndrome

Ellison and Zollinger,[1] in 1955, first drew attention to the syndrome of: (1) A diathesis towards fulminating peptic ulcer, (2) gastric hypersecretion, and (3) an islet-cell tumour of the pancreas *not* composed of β cells.

More recently it has been established that this syndrome may incorporate other features, namely, diarrhoea, steatorrhoea and hypokalaemia. These may precede ulcer symptoms by months or years and may in themselves determine a fatal outcome.[2] In the past few years numerous cases have been described. The sexes are equally affected and the commonest age group is that between 30 and 50 years. The ulcers have several characteristic features: (1) They may be multiple; (2) they may be in unusual sites, such as the 3rd part of the duodenum or in the jejunum; and (3) the course of the ulcers is fulminant and characterized by serious complications, rapid recurrence after normal adequate surgical treatment, and considerable weight loss—many patients have had more than one operation, several have

had 5 or 6 and most have eventually died from complications of peptic ulcer or its treatment.

In the untreated patient the volume and acidity of the gastric juice tends to be greater than that found with the usual duodenal ulcer. The resting juice often amounts to 2-3 litres in 12 hours, the pH is 1·4 and the mEq. per litre value is often above 100 (normal 20 mEq. per litre). The hypersecretion is not abolished by vagotomy, and in fact Zollinger and McPherson,[3] in 1958, advocated total gastrectomy.

More recently, however, less radical surgery seems to be indicated if the ulcerogenic tumour can be removed at the same time. Stammers[4] has shown that the removal of a non-beta-cell tumour of the pancreas in a patient presenting with diarrhoea, steatorrhoea and gastric hypersecretion had cured the patient. In two-thirds of the cases the tumour is in the body or tail of the pancreas. Often the tumour is so small that it is easily missed. On the other hand the tumours are often multiple and may even be in ectopic sites. It has been suggested that it may be wise to resect the distal two-thirds of the pancreas if a tumour is not found. If it is found in the head, enucleation may be possible. If not, pancreato-duodenectomy may be necessary.

The exact mechanism whereby ulceration in the upper gastro-intestinal tract is produced has not been definitely established, but facts gathered recently seem to point to a humoral agent of the nature of gastrin. Insulin can be ruled out because most patients with β-cell tumours do not have peptic ulceration, and hypoglycaemia is not found in the Ellison-Zollinger syndrome. Glucagon, the secretion of the γ-cells, is diabetogenic and it actually *inhibits* gastric secretion.[5]

Above all, in any patient presenting with the Ellison-Zollinger triad, a search should be made for *other* endocrine lesions. A glucose-tolerance curve should be obtained, an X-ray film of the pituitary fossa should be made, the serum-calcium and phosphate levels should be measured, the urinary tract should be X-rayed, and the adrenal-steroid excretion should be estimated. It has been shown that about 25% of cases of the Ellison-Zollinger syndrome have other endocrine adenomas. Ellison,[6] in a study of postmortem material, has shown an increased incidence of duodenal ulcer in diabetes mellitus, and a significant correlation between duodenal ulcer and the occurrence of adrenal cortical adenomas unaccompanied by any sign of hyper-cortism.[7]

Endocrine Aspect of Duodenal Ulceration

1. Gonads

The incidence of duodenal ulceration is much higher in men than in women, the ratio being 4 : 1. It has also been observed that ulceration symptoms frequently undergo marked changes during pregnancy and with the onset of the menopause.

2. Parathyroids

Approximately 25% of patients with hyperparathyroidism have peptic ulcers and a much greater percentage have gastro-intestinal symptoms. It is noted that, in hyperparathyroidism, there is (*a*) a much greater incidence of duodenal ulceration in women, (*b*) frequent absence of gastric hypersecretion, and (*c*) increased frequency of gastric ulcers in men.

3. Thyroid

Peptic ulceration is very uncommon in thyrotoxicosis. Hypochlorhydria or achlorhydria is often found in toxic goitre.

4. Pancreas

Whether diabetes predisposes to ulceration or not is controversial. Joslin's[8] experience is that ulceration is not commoner in diabetics, while Ellison, Abrams and Smith[6] are of the opinion that peptic ulceration is more frequent in diabetes.

5. Adrenals

In Addison's disease the gastric hydrochloric-acid level is low. Administration of ACTH and cortisone returns this level to normal. In cases of Curling's ulcer seen at autopsy there is invariably adrenal hypertrophy.[9] Ellison, in a survey of 812 gastro-intestinal ulcers in 20,000 consecutive autopsies, showed adrenal hyperplasia in 14%.

6. Multiple Endocrine Adenomata

Occasional cases have been described in the literature in which adenomata of various endocrine glands have been found simultaneously and have been associated with peptic ulceration.[10] The suggestion is that, owing to the failure of one of the target organ glands, the feed-back hyperplasia of the pituitary can produce hyperplasia of other end organs. The acid-peptic axis is stimulated directly through central activity and parietal-cell hyperplasia, or indirectly as a by-product of secretion of the adrenals, gonads or parathyroids. That the functional interdependence of the glands of the endocrine system may have an anatomical basis has been known as a postmortem-room curiosity for many years, but that this can be clinically significant is only now being recognized. It appears that some forms of peptic ulceration, and particularly the relentless fulminating types, are associated with a more complex pattern of pluri-glandular adenomatosis.[11]

The Parathyroids and Hyperparathyroidism

It is not intended to deal with the anatomy, embryology and surgery of the parathyroids, since this has been comprehensively dealt with in a fairly recent article in this *Journal*.[13] Certain facts pertaining to the physiology and pathology of the parathyroids will be dealt with, as well as the consideration of the diagnosis and differential diagnosis of hyperparathyroidism.

Physiology

At the present time there are two known actions of the parathyroid hormone: (1) The mobilization of calcium from the skeleton, and (2) inhibition of re-absorption of filtered phosphate by the renal tubules.

These two mechanisms are independent of each other. There is no known tropic hormone from the pituitary which has any regulating mechanism on these glands. The regulating mechanism appears to be the level of calcium and phosphorus in the plasma. It seems to be independent of any nervous control. The plasma calcium and phosphorus bear a reciprocal relationship to each other under normal physiological conditions.

The plasma-calcium levels lie between 9 and 11 mg. per 100 ml. Only slight deviations from the normal range are tolerated and if they occur they may produce severe symptoms and disease. This accurate maintenance occurs in spite of a very rapid dynamic equilibrium between the relatively small amounts of calcium in the extracellular fluid and the very much larger quantities in the bones. An important basic fact is that any *acute* changes in plasma level must take place in the equilibrium between the plasma and bone.[14] On the other hand, more chronic changes of calcium level can be induced by an alteration in either calcium absorption or excretion or both.

Dent[14] has simplified matters by attempting to summarize calcium metabolism by a simple diagram (Fig. 5). The

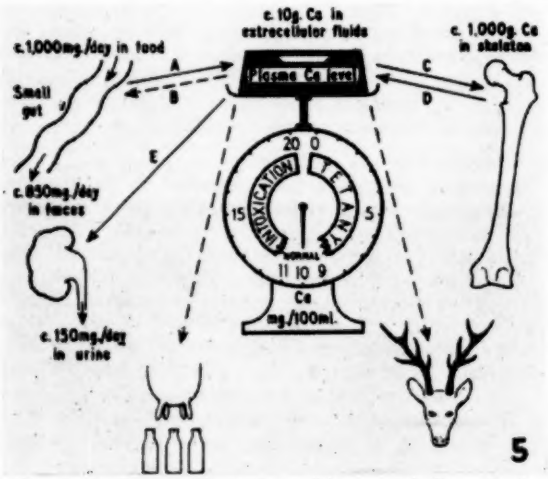

Fig. 5. A diagram illustrating calcium metabolism simply and concisely. [From: Dent, C. E. (1956): Proc. Roy. Soc. Med., **49**, 715.]

total serum-calcium concentration is dependent on the serum-protein concentration; for this reason the levels of both must be determined. The calcium bound to protein (5 mg. per 100 ml.) varies with the alterations in the serum-protein level and is not primarily affected by parathormone. In contrast, ionic calcium, 5 mg. per 100 ml., is specifically affected. Lowered serum proteins with normal serum calcium may indicate a raised ionic calcium from hyperparathyroidism. Although the ionic calcium and protein-bound calcium fractions cannot be determined individually, their relative concentrations can be determined. For example, the hypercalcaemia of multiple myeloma or sarcoidosis would be found to be associated with a rise in serum proteins.

Phosphorus metabolism is in some ways similar to calcium. They bear a reciprocal relationship to each other and they are both directly concerned with the formation of bone salts. They do, however, differ in that only half the total body store of phosphorus is in the skeleton, the rest being in the cells throughout the body. Also, acute changes in plasma phosphorus over a wide range do not appear to produce in themselves any symptoms or disease. The threat of poor absorption of phosphorus from the gut (as may happen with calcium) does not occur, since the supply and absorption is nearly always far in excess of body requirements. The normal kidney has a sharp threshold for phosphorus, and plasma levels do not alter with varying intake.

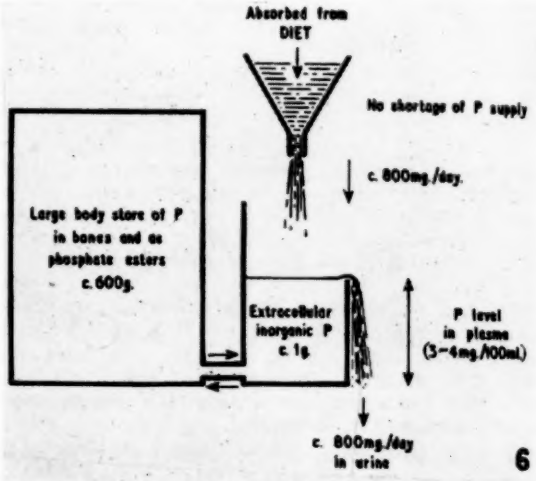
Absorbed from DIET
No shortage of P supply
c. 800mg./day.
Large body store of P in bones and as phosphate esters c. 600g.
Extracellular inorganic P c. 1g.
P level in plasma (3-4mg./100ml.)
c. 800mg./day in urine
6

Fig. 6. A diagram illustrating phosphorus metabolism. [From: Dent, C. E. (1956): Proc. Roy. Soc. Med., **49**, 715.]

Chronic changes in plasma level, therefore, reflect changes in renal function rather than changes in supply. Dent[14] has again brilliantly illustrated phosphorus metabolism by a simple diagram (Fig. 6).

Pathology

Somewhat more than 80% of hyperparathyroidism results from a single adenoma; less than 10% from multiple adenomata, and about 10% from hyperplasia of all the parathyroids. Malignant tumours are fortunately rather rare, accounting for not more than 1 - 2% of cases. Adenomata vary in size from tumours as large as a normal parathyroid gland to tumours the size of the thyroid lobe. The average size is unfortunately not very large; this makes exposure and discovery difficult.

In over 80% of cases the tumour is in one or other of the upper pair of parathyroid glands. The adenoma may arise in an aberrant parathyroid in the mediastinum, not infrequently in the thyroid, and rarely behind the oesophagus. The adenoma is oval, soft, smooth, encapsulated, and reddish-brown in colour, especially on the cut surface. In primary hyperplasia all the glands are involved, but not always symmetrically, so that macroscopically one or even two glands may seem involved. They appear somewhat more chocolate-brown than the adenomata, and their size and form vary greatly. There is no connection between the intensity of the hyperparathyroid state and the mass of the hyperplastic tissue.

Microscopically, the most striking feature in adenomata is the virtual absence of stromal fat which makes up 40 - 60% of the bulk of normal parathyroid tissue. There is a mixture of chief cells, water-clear cells and oxyphil cells in varying proportions. Often one may predominate and the adenoma may consist mainly of chief cells or water-clear cells. Oxyphil-

cell adenomata do not appear to produce hyperparathyroidism. Acini containing colloid may be present, so that if the tumour is embedded in the thyroid gland it may be mistaken for a thyroid adenoma. In hyperplasia the cells are all of one type—usually water-clear cells ('wasserhelle'). These cells are often much larger than normal, sometimes being 40 microns in diameter. Carcinoma is one of the rarest of tumours. It grows rapidly, infiltrates the thyroid gland, muscle, and the trachea and metastasizes to the regional lymph nodes, the lungs and the bones. It may produce parathormone, but does not often cause hyperparathyroidism. Microscopically, the usual signs of malignancy are present, i.e. the variability in size of cells and nuclei, and mitoses.

Diagnosis

Hyperparathyroidism may be either primary or secondary. In primary hyperparathyroidism the diverse manifestations of the disease may be caused by more than one type of hormone. In one type, the symptoms are those of hypercalcaemia and hypercalciuria without bone involvement. In the other type the symptoms may be the same, but in addition the skeleton always shows some radiological change, either local or generalized. Primary hyperparathyroidism, resulting from adenoma of the parathyroid, is not uncommon, and is a potentially fatal disease which is curable in most cases if treatment is instituted before progressive renal disease develops. Diagnosis is rarely made before complications involving, in the majority of cases, the skeleton or urinary tracts, have developed.

In the skeleton, generalized or localized osteitis fibrosa cystica may occur, although this is unusual, whereas complications in the urinary tract are common. Probably 5% of all radiopaque renal stones and probably 15% of cases of recurrent lithiasis result from hyperparathyroidism. It is a widespread belief that a *sine qua non* for the diagnosis of hyperparathyroidism is some form of bone lesion, and this may be one of the reasons why an accurate diagnosis of hyperparathyroidism is not often made. In addition, it is well to remember that hypercalcaemia is not always constantly present in this condition. The symptom complex falls into three categories: (1) The result of high blood calcium, (2) excessive urinary calcium and phosphorus, and (3) secondary bone changes.

In the absence of any specific bone or renal lesion the diagnosis can only be made and confirmed by blood chemistry, since the symptoms simulate many functional disorders. They include: muscle weakness and abnormality of gait, vaguely localized pain, fatigue, anorexia, nausea, vomiting, loss of weight, constipation, lethargy, bradycardia and cardiac irregularities.

Muscle weakness is often the precursor of the typical bone changes that occur in this condition. It varies from a general feeling of tiredness to a degree of extreme weakness in which the patient is bedridden and can only lie on his back and is unable to move his limbs. Once bone changes have occurred and bone pain is conspicuous, the muscular weakness is easily explained by the pain produced on movement. Associated with this weakness patients may have abnormal gaits. The only striking one is the waddling gait which may occur in many surgical diseases. Its commonest cause is probably coxa vara from softening of the femoral neck, but it may be seen before any bone changes take place and is possibly caused by weakness of the gluteal muscles. Vaguely localized pains, although common, with already existing bony changes, may precede them. In adults the commonest site is in the lower back, followed closely by pains in the hips and down the middle of the legs.

Osseous complications of hyperparathyroidism vary from minimal decalcification, which may be asymptomatic, to a full-blown osteitis fibrosa cystica. Localized cysts, giant-cell tumours, and fractures may be so prominent that sight is lost of the generalized lesion. The alkaline phosphatase is usually raised only when the bone lesions are radiologically visible. Pathognomonic features, radiologically, are subperiostial resorption of bone in the long bones (especially the metacarpals and phalanges) and the absence of the lamina dura of the teeth.

The kidney, as would be expected, is the main target for the abnormal calcium metabolism. The calcium freed into the blood is excreted by the kidneys in the urine. The excess calcium tends to be deposited in the urinary tract. The renal changes most easily recognized are calculus formation and nephrocalcinosis. Renal changes may occur with or without skeletal lesions. Commonly found with marked bony changes are soft, often bilateral, phosphatic calculi, at times so extensive as to show on X-ray as cysts of the renal pelvis. These are the stones that are likely to disappear after removal of the parathyroid adenoma. On the other hand, the widely diffused calcific deposits throughout the renal parenchyma—nephrocalcinosis—do not disappear after removal of the parathyroid adenoma. Following on these widespread changes, clinical hypertension may develop, and with it the train of events that follow on renal failure. The patient with a renal stone resulting from a parathyroid adenoma has less chance of normal health, and even of survival, than has the patient with idiopathic renal stone. It is therefore important that a possible diagnosis of hyperparathyroidism should be considered in every patient with a calcium-containing renal stone.

Primary disturbance of bone formation, although at one time thought to be the commonest manifestation of this

TABLE I. SERIES OF CASES OF PRIMARY HYPERPARATHYROIDISM PUBLISHED BETWEEN 1948 AND 1954[17]

Type	*Albright and Reifenstein (1948)*	*Burk (1948)*	*Lahey and Murphy (1953)*	*Richardson (1953)*	*Black (1953)*	*Hellstrom (1954)*	*Total*
Skeletal changes alone	11	3	16	—	16	13	59
Skeletal changes with nephrocalcinosis or renal calculi	24	7	9	7	16	10	66 (±7)
Nephrocalcinosis or renal calculi alone	28		4	4	73	27	136 (±7)
Neither skeletal changes nor calculi ..	1	—	—	—	7	—	8
Total	64	10	29	11	112	50	276

condition, has now taken second place to renal changes. In a summary of the world literature from 1947 to 1954, Pyrah's figures[17] show that there were 166 cases with primary renal changes compared with 66 cases with primary bone changes (Table I). The well-known bone changes of generalized osteitis fibrosa cystica (von Recklinghausen's disease) are the least common manner of presentation today. Single osteoclastomata or cysts, most commonly of the jaw, may be the only presenting sign. On the other hand, symptoms and signs may be most confusing and the distinction from other more purely orthopaedic conditions may be exceedingly difficult. Mention has already been made of vague localized pain in the back and legs, and the abnormality in gait. Pathological fractures bring a host of aetiological factors to mind; fortunately X-ray examination and biochemical analysis of the blood leave few undiagnosed. Kyphosis and scoliosis may produce reduction in the total stature of adults. Dent[14] suggests that any adult whose expected height is about 10 inches below normal should be considered as possibly having bone disease until proved otherwise. Whereas renal changes are not often reversible, most of the bone lesions are, once the parathyroid adenoma has been removed.

Among the less well-known modes of presentation are recurrent peptic ulceration and pancreatitis. The importance of recognizing the co-existence of peptic ulceration in cases of hyperparathyroidism is stressed by Alvarez *et al.*[18] They point out that treatment with antacids and milk leads to heightened calcium intake which might well push the patient into an acute stage of hyperparathyroidism, with possible fatal results. The problem is made more difficult by the fact that nausea, abdominal pain and vomiting are symptoms of primary hyperparathyroidism and may closely mimic the symptoms of peptic ulceration. More understandable is the occurrence of arterial thrombosis, where ectopic calcification in the arterial wall and increased coagulability of the blood both play their part.

Up to now only primary hyperparathyroidism has been considered, but hyperparathyroidism (secondary) may occur as a compensatory mechanism under certain circumstances and, if the march of events is not halted, may become indistinguishable from primary hyperparathyroidism. Hyperplasia, which may go on to adenoma formation, occurs secondarily to a fall in serum calcium or a rise in serum phosphorus, and may be classified thus:

1. When the serum-calcium level falls, caused by—
(*a*) deficient intake, or
(*b*) deficient absorption, resulting from (*i*) deficiency of Vitamin D (rickets, osteomalacia); (*ii*) resistant rickets; (*iii*) steatorrhoea; (*iv*) gastrectomy; (*v*) small-bowel resection; (*vi*) biliary obstruction; (*vii*) excessive phytic acid in diet; (*viii*) pancreatic insufficiency; or (*ix*) old age.
2. When the serum-phosphorus level rises, caused by—
(*a*) chronic glomerular nephritis, or
(*b*) Fanconi's syndrome.

It may be pointed out that in chronic renal failure patients occasionally present with symptoms of bone disease, while primary hyperparathyroidism is often associated with chronic renal failure. The distinction is not always easy although very important, since the treatment in one case is medical, and in the other, surgical. An interesting table, drawn up by Dent,[14] indicates the biochemical changes that can occur in various conditions which may be confused with primary hyperparathyroidism (Table II).

It is well documented that surgery for primary hyperparathyroidism is usually successful and that recurrence is rare; so much so that persistence or reappearance of symptoms and high serum-calcium levels has come to be regarded as evidence of inadequate surgical therapy. There is no doubt that the greater awareness of the early symptoms and signs of hyperparathyroidism on the part of the medical profession is helping an earlier diagnosis of these patients before the relentless progress of renal failure has taken place.

The present case helps to re-emphasize the truism that these rather uncommon conditions will rarely be diagnosed unless they are *borne in mind* when dealing with signs and symptoms that defy the usual routine medical care. Here, more than ever, the cooperation and integration between clinician, radiologist and biochemist will be of maximum benefit.

CONCLUSION AND SUMMARY

The relentless progress of gastroduodenal ulceration which did not respond to routine surgical treatment led to the wrong conclusion that an ulcerogenic tumour of the pancreas was present. Ellison and Zollinger first discovered this syndrome in 1955. It consists of: (1) A fulminating ulcer diasthesis, (2) marked gastric hypersecretion, and (3) a non-β-cell tumour of the pancreas.

In the case reported there was no gastric hypersecretion. With the knowledge that these cases may have some other endocrine basis, further tests were done and the serum calcium was found to be markedly raised. This led to the

TABLE II. BIOCHEMICAL CHANGES IN METABOLIC BONE DISEASES[14]

Disease	*Plasma calcium* (*mg./100 ml.*)	*Plasma phosphorus* (*mg./100 ml.*)	*Plasma bicarbonate* (*mEq./l.*)	*Blood urea* (*mg./100 ml.*)	*Alkaline phosphatase* (*K-A units*)	*Urine calcium* (*mg./24 hrs.*)
Normal (adult)	9 - 11	3 - 4	24 - 28	20 - 35	5 - 12	120 - 220
Idiopathic osteoporosis	normal	normal	normal	normal	normal	(high if in an active phase)
Primary hyperparathyroidism	11 - 16	1 - 3	normal	normal	15 - 100	300 - 800
Chronic renal failure	6 - 11	4 - 12	10 - 22	50 - 400	15 - 100	50 - 200
Renal-glomerular osteodystrophy						
Secondary hyperparathyroidism						
Rickets or osteomalacia, any origin, non-acidotic	8 - 10	1 - 3	20 - 28	normal	5 - 50	10 - 100
Rickets or osteomalacia, acidotic	7 - 11	1 - 4	10 - 22	30 - 80	15 - 50	150 - 350
Hypophosphatasia	9 - 15	4 - 8	20 - 28	20 - 100	1 - 2 (adult) 3 - 8 (infant)	Insufficient data, probably high normal or high

biochemical confirmation that the aetiological factor was a parathyroid lesion. This was proved by operation and microscopy.

The physiology and pathology of hyperparathyroidism are dealt with, and the diagnosis and differential diagnosis are discussed. Finally, the point is stressed that these conditions will only be diagnosed if kept in mind in dealing with patients with chronic ill health who do not respond to routine medical care.

I should like to thank Dr. J. Tanchel, Medical Superintendent of the Addington Hospital, and Mr. A. Copley, who was in charge of this patient. I am also grateful to Mr. C. R. Stewart of the Photographic Unit, Department of Pathology, University of Natal. Thanks are also due to the editors of the *Proceedings of the Royal Society of Medicine* and to Profs. C. E. Dent and L. N. Pyrah for permission to reproduce Table I (Professor Pyrah) and Table II (Professor Dent) and Figs. 5 and 6 (Professor Dent).

REFERENCES

1. Zollinger, R. M. and Ellison, E. H. (1955): Ann. Surg., **142**, 709.
2. Leading Article (1960): Lancet, **2**, 137.
3. Zollinger, R. M. and McPherson, R. C. (1958): Amer. J. Surg., **95**, 359.
4. Stammers, F. A. R. (1960): Lancet, **2**, 131.
5. Clarke, S. D., Heill, D. W. and Welbourne, R. B. (1960): Gut, **1**, 86.
6. Ellison, E. H., Abrams, J. and Smith, D. (1959): Amer. J. Surg., **97**, 17.
7. Moore, F. D. (1960): Surgery, **48**, 170.
8. Joslin, E. P. (1937): *The Treatment of Diabetes Mellitus*, 6th ed. Philadelphia: Lea and Febiger.
9. Moore, F. D. (1957): Recent Progr. Hormone Res., **13**, 511.
10. Underdohl, L., Woolner, L. and Black, B. M. (1953): J. Clin. Endocr., **13**, 20.
11. Leading Article (1959): Lancet, **1**, 133.
12. Bradlow, B. A. and Segel, N. (1956): Brit. Med. J., **2**, 197.
13. McGregor, A. L. (1959): S. Afr. Med. J., **33**, 5.
14. Dent, C. (1956): Proc. Roy. Soc. Med., **49**, 715.
15. Boyd, W. (1955): *Pathology for the Surgeon*. Philadelphia and London: W. B. Saunders.
16. Black, B. M. (1958): Amer. J. Surg., **95**, 395.
17. Pyrah, L. N. (1956): Proc. Roy. Soc. Med., **49**, 722.
18. Alvarez, A. F., Stefanelli, J. and Crawford, D. J. M. (1956): Brit. J. Surg., **44**, 193.

A COMPARATIVE STUDY OF FLUID VOLUMES IN HEART-LUNG BY-PASS OPERATIONS IN OPEN-HEART SURGERY

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Those concerned with the management of patients undergoing open-heart operations in Johannesburg have had to find their own solution for the control of fluid volume in heart-lung by-pass operations, on account of the particular climatic conditions prevailing in this city. Johannesburg is situated 6,000 feet above sea level. During the mid-winter month of July 1960, the mean noon humidity mixing ratio was 4·5 G. of water in 1 kg. of air. The minimum temperature was 4·5°C. and the maximum temperature 16°C. During the mid-summer month of January the mean noon humidity mixing ratio was 12 G. of water in 1 kg. of air. The minimum temperature was 16°C. and the maximum temperature 24°C.[1] Although the operating theatre was air-conditioned, the room in which the patient was nursed was not so controlled.

It was hoped to develop a régime for our climate with which all who were concerned with the care of patients could become conversant. The advantages of such a régime were felt to lie in the formulation of a normal course of events that would enable abnormalities to be readily detected.

Two series of consecutive patients were studied to test the reproducibility of results and to bring out the differences produced by the administration of different quantities of fluid. The first series consisted of 25 patients and the second of 40 patients. In the first series the average size of the patients was 1·27 square metres body surface area (sq. m. BSA).[2] The volumes of blood and 5% dextrose in water administered were restricted to a minimum in an attempt to establish what advantages, if any, lay in stringent fluid restriction. In the second series the average size of the patients was 1·19 sq. m. BSA and larger quantities of blood and 5% dextrose in water were administered.

BLOOD LOSS

In the first series, during operation the average volume of blood lost per sq. m. BSA was 995 ml. This included 707 ml. lost into the suction sump, 111 ml. removed for tests, 119 G. lost on the swabs and 58 G. lost in spillage. The volume of blood replaced was 1,156 ml. per sq. m. BSA, giving a positive balance of 162 ml. per sq. m. BSA at the end of the operation.

In the second series the average volume of blood lost during the operation was 1,040 ml. per sq. m. BSA. 778 ml. were lost into the suction sump. Since fewer tests were done, only 70 ml. were removed for tests. The quantity lost on the swabs was 125 G. and that spilt was 67 G. The average volume of blood replaced was 1,388 ml. per sq. m. BSA, giving a positive blood balance of 348 ml. per sq. m. BSA at the end of the operation.

It had become apparent that mere replacement of the blood lost did not always result in a satisfactory postoperative state. The volume of blood replaced must ensure a systemic blood pressure, as near as possible to the pre-operative pressure, and a satisfactory venous pressure in the neighbourhood of 15 cm. of water. It is desirable that the venous pressure be maintained at 15 cm. of water irrespective of whether the volume of blood in the patient is greater or less than before operation. There is no relationship between the size of the patient and the volume of blood lost during the operation (Fig. 1).

Nearly all the blood lost in the postoperative period was lost in the first postoperative 24 hours. In series 1 the average volume of blood lost was 865 ml. per sq. m. BSA in the first 24-hour period, and 126 ml. per sq. m. BSA in the second 24-hour period. The total postoperative blood loss was 991 ml. per sq. m. BSA. The volume of blood replaced in the corresponding postoperative period was 1,153 ml. per sq. m. BSA, showing a postoperative positive balance of 162 ml. per sq. m. BSA.

In series 2 the average blood loss was 763 ml. per sq. m. BSA in the first postoperative 24-hour period. The average blood loss in the second postoperative 24-hour period was 105 ml. per sq. m. BSA. The total postoperative blood

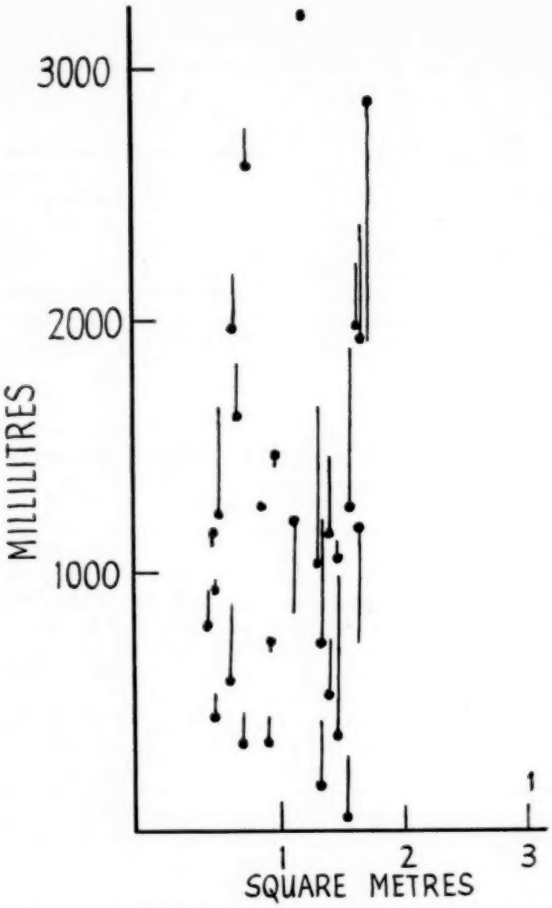


Fig. 1. Volumes of blood lost and replaced in each patient during heart-lung operations. The dot denotes the volume of blood lost and the point at the end of the vertical line the volume replaced.

loss was 868 ml. per sq. m. BSA. The distribution of this loss in the individual patients is illustrated in Fig. 2. The average volume of blood replaced in the first 24-hour period was 956 ml. per sq. m. BSA and in the second postoperative 24-hour period 128 ml. The average volume of blood replaced in the postoperative period was 1,084 ml. per sq. m. BSA, showing a postoperative positive blood balance of 216 ml. per sq. m. BSA.

The average positive blood balance during the postoperative period showed an increase from 162 ml. per sq. m. BSA in series 1, to 216 ml. per sq. m. BSA in series 2. Two possible explanations exist for the smaller blood loss in the second series. These are, increased experience in the surgical procedure and the substitution of polybrene for protamine to reverse the effect of heparin.[3]

Although the blood loss during the operation is unrelated to the patient's size, the blood loss during the postoperative period increases with the size of the patient. The greater blood loss in the bigger patients, noted over the whole operative and postoperative period is, therefore, ascribable to the greater loss by the bigger patients during the postoperative period.

The average total volumes of blood lost during the combined operative and postoperative periods in series 1 and 2 showed a remarkable constancy at 1,986 ml. per sq. m. BSA and 1,908 ml. per sq. m. BSA respectively. The average total volumes of blood replaced in series 1 and 2 were 2,309 ml. per sq. m. BSA and 2,472 ml. per sq. m. BSA respectively. Conforming to the principle of maintaining the arterial and venous blood pressures, besides replacing blood loss, the positive average balance of 323 ml. per sq. m. BSA in series 1 was increased to 564 ml. per sq. m. BSA in series 2 over the whole procedure. The final blood balance is nearly always positive and is not related to the patient's size.

FLUID BALANCE

Intravenous Fluid

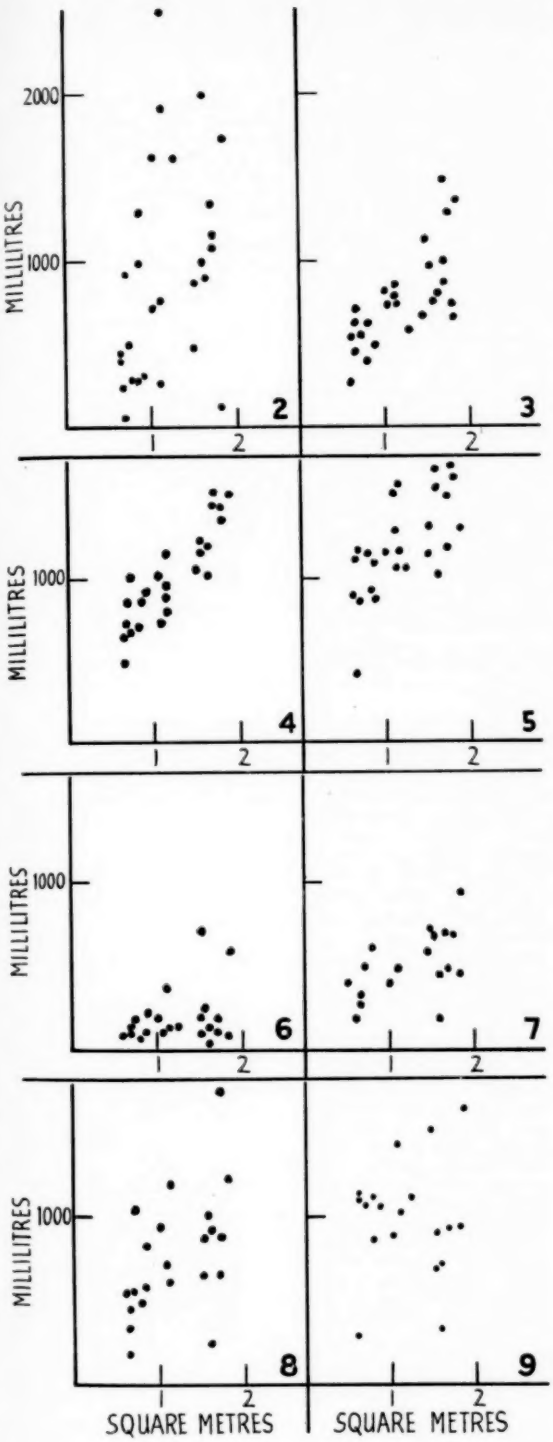
In series 1 the average volume of 5% dextrose in water administered during the operation was 125 ml. per sq. m. BSA. The average volumes of 5% dextrose in water administered per sq. m. BSA for the first, second and third postoperative 24-hour periods were 524 ml., 690 ml., and 727 ml. respectively. The distribution of these volumes in relation to the sizes of the patients was described previously.[4] The average total volume of 5% dextrose in water administered per sq. m. BSA during the operative and postoperative 72 hours was 2,066 ml.

In series 2 the average volume of 5% dextrose in water administered per sq. m. BSA during the operation was 430 ml. During the first, second and third postoperative 24 hours the volumes per sq. m. BSA were 692 ml., 892 ml., and 1,048 ml. respectively. The distribution of these volumes in relation to the sizes of the patients is illustrated in Figs. 3, 4 and 5. The average total volume administered during the period of operation and the ensuing postoperative 72 hours was 3,062 ml. per sq. m. BSA. Thus a total of 996 ml. per sq. m. BSA more was administered in series 2 than in series 1.

Urine

Immediately before going for operation each patient was made to pass urine. In series 1 the average volumes of urine passed per sq. m. BSA in the first, second and third postoperative 24-hour periods were 505 ml., 562 ml., and 505 ml. respectively, giving an average total urine output from the beginning of the operation to the end of the 72nd postoperative hour of 1,572 ml. The distribution of these volumes in relation to the sizes of the patients has been described previously.[4] The average volume of 5% dextrose in water administered during this same period was 2,066 ml. per sq. m. BSA. The positive balance of 5% dextrose in water above the urine excreted was 494 ml. per sq. m. BSA.

In series 2 the patients were catheterized at the end of the operation, and the average volume of urine obtained was 145 ml. per sq. m. BSA. The distribution of these volumes in relation to the sizes of the patients is illustrated in Fig. 6. The volume of urine excreted during the operation bears no relation to the size of the patient. The aver-



age volumes of urine secreted per sq. m. BSA in the first, second, and third postoperative 24-hour periods were 430 ml., 688 ml., and 865 ml. respectively. The distribution of these volumes in relation to the sizes of the patients is illustrated in Figs. 7, 8 and 9. The volume of urine passed from the beginning of the operation to the end of the 72nd postoperative hour was 1,983 ml. per sq. m. BSA. The volume of 5% dextrose in water administered during this period was 3,062 ml. per sq. m. BSA. The positive balance of 5% dextrose in water administered above the urine excreted was 1,079 ml. per sq. m. BSA.

In series 1 the average specific gravity of the urine during the first, second, and third postoperative 24-hour periods was 1023, 1023, and 1019 respectively. In series 2 the corresponding average specific gravity was 1020, 1016, and 1012 respectively.

No attempt has been made to assess the quantity of fluid produced by metabolism in the patients. On account of the many difficulties involved no attempt has been made to evaluate the insensible fluid loss.

COMMENT

In series 1 the positive blood balance at the end of the operation was 162 ml. per sq. m. BSA. In series 2 this figure was raised to 216 ml. per sq. m. BSA, which resulted in more satisfactory venous and systemic blood pressures. In series 1 at the end of the 72nd postoperative hour the total positive blood balance was 323 ml. per sq. m. BSA, and in series 2, 564 ml. per sq. m. BSA. The condition of the patients in series 2 gave rise to much less anxiety during the postoperative period. In series 1 the average total of 5% dextrose in water administered from the beginning of the operation to the end of the 72nd postoperative hour was 2,066 ml. per sq. m. BSA. The corresponding volume in series 2 was 3,062 ml. per sq. m. BSA, an increase of 996 ml. per sq. m. BSA.

The increase in blood administered and the 5% dextrose in water increase of 996 ml. per sq. m. BSA in series 2 was sufficient to reduce the average specific gravity of the urine in the first postoperative 24 hours from 1023 to 1020, in the second postoperative 24 hours from 1023 to 1016 and in the third postoperative 24 hours from 1019 to 1012.

The fact that in series 1 the volume of urine remained more or less constant at about 500 ml. per sq. m. BSA

Fig. 2. Total postoperative blood loss, per patient.
Fig. 3. Fluid intake (5% dextrose in water), per patient, in first postoperative 24 hours.
Fig. 4. Fluid intake, per patient, in second postoperative 24 hours.
Fig. 5. Fluid intake, per patient, in third postoperative 24 hours.
Fig. 6. Catheter urine, per patient, obtained at the end of operation.
Fig. 7. Urine output, per patient, during operation and in first postoperative 24 hours.
Fig. 8. Urine output, per patient, in second postoperative 24 hours.
Fig. 9. Urine output, per patient, in third postoperative 24 hours.

Figs. 2-9 refer to patients from series 2. Although this was a series of 40 unselected cases, some of the patients died, some of the patients were incontinent, and some of the urines collected were accidentally spilt; therefore data were not available for all patients in the series. Thus, the number of patients represented in the various graphs is not constant.

for the first 3 periods of 24 hours, would indicate that the patients were excreting an obligatory urine and were, therefore, being dehydrated. In series 2 the volume of urine showed an increase in each of the successive 3 periods of 24 hours, indicating that they were receiving sufficient fluid to allow them to excrete a volume of urine in excess of an obligatory urine. The fact that the average specific gravity did not fall below 1012 suggests that the patients were not being overhydrated. It appears that the balance struck was satisfactory. Fewer of the patients in series 2 complained of thirst than in series 1.

SUMMARY

The control of blood and fluid volumes in 2 series of 25 and 40 consecutive patients undergoing open-heart surgery on the heart-lung oxygenator are compared. Volumes which have been found to give satisfactory postoperative results have been established.

I wish to thank the thoracic surgeons Mr. D. I. Adler, Mr. L. A. du Plessis, Mr. L. Fatti, Mr. D. N. Fuller and Mr. P. E. Marchand for allowing access to their patients; also the physicians, Dr. J. L. Braudo, Dr. M. M. Zion, and Dr. J. Barlow; the anaesthetists, Dr. F. J. Durham, Dr. C. Frost, Dr. K. B. Meaker, Dr. J. Pitcher and Dr. C. H. van Hasselt; the pathologists, Dr. H. B. W. Greig and Dr. A. Walker; and Sister H. du Preez, for their help.

REFERENCES

1. African Climatology Unit, University of the Witwatersrand, Johannesburg: Personal communication.
2. du Bois, E. F. (1936): *Basal Metabolism in Health and Disease*, 3rd ed. London: Ballière, Tindall and Cox.
3. Rothnie, N. G. and Kinmonth, J. B. (1960): Brit. Med. J., **1**, 73.
4. Scott, W. F. (1960): S. Afr. Med. J., **34**, 249.

NATIONAL CANCER ASSOCIATION OF SOUTH AFRICA: PRESIDENT'S ADDRESS*

LEWIS S. ROBERTSON, M.B., CH.B., D.P.H.

The National Cancer Association of South Africa is a voluntary organization devoted to promoting the campaign against cancer in its research, therapeutic and preventive aspects. Its aims and objectives are to advance scientific research on the causes, diagnosis and treatment of cancer, to encourage the extension of diagnostic and treatment services in the main hospitals in South Africa, to improve undergraduate and postgraduate teaching of oncology, to propagate knowledge about cancer, and to combat charlatanism.

It is affiliated to the Union-Internationale Centre le Cancer (UICC), an international organization with similar aims and objects, and the British Empire Cancer Campaign, an organization carrying out intensive cancer research.

It is my privilege to report on another year during which the National Cancer Association of South Africa has made steady progress in its four-pronged programme of *research, the dissemination of professional information, public education* and *assistance to cancer sufferers.*

Members have received copies of the 1960 annual report, together with the audited accounts for the year. Attention is directed to a few salient features.

The Cancer Association and the Medical Profession

When the Association originally laid the foundations for its programme, it realized that the medical profession would have to play an important rôle if the fight against cancer were to meet with success. It is appreciated that members of the medical profession are confronted with a diversity of problems found in few other professions. The general practitioner is faced each day with varying forms of illness ranging from minor to major conditions. The Cancer Association's main task is to furnish doctors with information on the differential diagnosis of the various forms of cancer and the latest available knowledge in regard to treatment. It has to keep the subject of cancer constantly before the doctors. Where it considered that world advances in the diagnosis and treatment of cancer warranted it, doctors were encouraged to obtain specialized instruction overseas so that, among other things, it would ultimately be unnecessary to send cancer patients overseas for treatment. These aims have been achieved in various ways.

The South African Cancer Bulletin, a quarterly publication, now in its sixth year of production, not only reaches all practising doctors in the country, but has also been distributed free of charge to all final-year medical students. Each year's crop of qualified doctors has therefore been 'indoctrinated' with the cancer message.

Probably the most useful contribution made by the Cancer Association was in bringing pertinently to the notice of the medical profession the great value of the early diagnosis of uterine and other forms of cancer by means of the exfoliative cytology technique of cell examination. Certain doctors were awarded grants to obtain specialized training overseas and they, in turn, are training colleagues. Doctors, so trained, have conducted a full-time course for the training of cyto-technologists — laboratory assistants who are rendering useful services under the supervision of pathologists and gynaecologists.

The Association made a major contribution in financing the training overseas of doctors and physicists responsible for operating the cobalt bomb in the treatment of cancer patients. It has established a Tumour Reference Panel which renders valuable service in the diagnosis of difficult and doubtful tumours.

Specialists in various cancer fields visit outlying areas to lecture to doctors on the latest advances in diagnosis and treatment techniques. Professional films imported by the Association have brought within the reach of doctors and medical students films of intricate cancer operations.

The efforts of the Cancer Association combined with the normal progress made by the medical schools and other teaching institutions are such that the Association is able to say that it should seldom be necessary to send cancer patients overseas for cancer treatment.

Applications for Financial Assistance to Undergo Treatment Overseas

From time to time instances have been reported in South African newspapers of patients, suffering from certain forms of cancer, proceeding overseas for treatment. The implications of these journeys are of interest to the general public as well as to the individual concerned.

In situations of this kind it is wise to look at the issue objectively and not be carried away by emotion. Obviously, the crucial question to be answered is whether or not the treatment can be carried out in South Africa. It can be said quite categorically that facilities and personnel exist in South Africa which enable highly complicated surgical operations and other procedures to be carried out. There may, however, be occasions when overseas facilities may be sought in exceptional instances.

In the event of an appeal being made to the National Cancer Association to assist financially in sending anyone to another country to undergo treatment for cancer, the Association's policy is to obtain authoritative information concerning the medical history of the patient and medical opinion on the necessity and wisdom of the proposal; and whether or not the treatment is available in South Africa. It considers it would be preferable that the patient be not informed of the proposal before the matter has been considered and a decision made. It is cruel to raise false hopes unnecessarily, as might happen through over-enthusiasm.

South Africa is well equipped to deal with all aspects of the

* Delivered at the Annual General Meeting of the National Cancer Association of South Africa on 28 August 1961.

medical treatment of the human body, and it is only in the most exceptional case that overseas treatment would be supported.

Public Education

Because the development of cancer is usually painless, and early cancers can often be cured, it stands to reason that the Association leaves no stone unturned to ensure that patients consult their doctors at the earliest possible stage of the disease. This can best be done by educating the public to recognize the early and painless symptoms of cancer. Most gratifying results are being achieved, as is shown by the fact that more and more cancers are being discovered in the early stages, resulting in more cures being effected. The annual report contains significant statistics about the increasing number of people being reached from year to year by means of the Association's various educational methods.

I would be failing in my duty if I did not pay tribute to the alertness of South African womanhood to the dangers of cancer. Women's organizations are playing an increasingly important rôle in disseminating and absorbing cancer educational material. Small wonder then that South African women as a group are becoming the staunchest supporters of the Association's programmes. It is fitting, therefore, that the Association decided to embark during 1961 on a campaign against uterine cancer which holds out the real hope that, with the cooperation of women, this form of cancer may within a few years be a minor cause of death.

The Cancer Association is deeply concerned about the misery and suffering caused by cancer quacks, whose most fruitful field of operation is usually limited, and ironically so, to skin cancer, which is the most easily curable form of cancer. The annual report concerns itself with an urgent appeal to the victims of quacks, and I particularly direct the attention of the Press to the humane service which could be rendered to these unfortunate individuals by giving publicity to this appeal.

General

An innovation has been introduced in the 1960 annual report by including reports on the activities of Branches of the Association. Branches are assuming more and more responsibility in their own areas and I would like to congratulate and thank the personnel of Branch Councils and their Committees for the active and lively interest they have taken during 1960 and to express the hope that they will proceed from strength to strength.

The Cancer Association continued to pursue its cancer research programme vigorously during the year under review. Attention is directed to the section in the annual report, which deals comprehensively with research sponsored by the Association.

With regard to finance it will be observed from the explanatory paragraph on pages 26 and 27 of the Annual report that there was an excess of £16,046 (R32,092.00) of expenditure over income during the year. It is earnestly hoped that increasing support from the public of South Africa will enable the Council of Management to close the gap in its annual budget.

In conclusion, I wish to express my personal and sincere appreciation to my colleagues on the Council of Management and those serving on committees thereof for their support and cooperation during the past year, and to record the Association's thanks to the Secretary and staff for their loyal and efficient service in spite of the ever-increasing burden placed upon their shoulders with the great expansion of the Association's activities.

UNIVERSITEITSNUUS : UNIVERSITY NEWS

PROFESSOR OF RADIOTHERAPY

Dr. Theunis Fichardt, M.D., D.Sc., M.Med. (Rad. T.), D.M.R.E., is so pas bevorder van Senior Lektor en Hoof van die Departement Radioterapie tot Professor in die Radioterapie aan die Universiteit van Pretoria en die Algemene-hospitaal, Pretoria. Professor Fichardt is in bevel van die eerste 2,000-curie telekobaltbom wat in 1959 in Suid-Afrika geïnstalleer is vir die behandeling van diep-geleë kankers.

Dr. Theunis Fichardt has been promoted from Senior Lecturer and Head of the Department of Radiotherapy to Professor of Radiotherapy at the University of Pretoria and the Pretoria General Hospital. Professor Fichardt is in charge of the first 2,000-curie telecobalt bomb which was installed in South Africa in 1959 for the treatment of deep-seated cancer.

Professor Fichardt

Professor Fichardt was born at Bloemfontein on 29 December 1907 and educated at Grey College (1919 - 1925). After matriculation he studied law for 1 year at Grey University College, and played rugby for the University First XV and for Free State in 1926. During 1927 and 1928 he played rugby for the Witwatersrand University First XV and for Transvaal. In 1928 he was selected to take part in the Springbok rugby trials in Durban, but an attack of pneumonia prevented him from making full use of this opportunity.

In 1927 he went to the University of the Witwatersrand to study medicine. There he completed the first and second years of the course and completed his medical studies overseas.

In London he qualified M.R.C.S. (Eng.), L.R.C.P. (Lond.) from Guy's Hospital in June 1933. After qualifying he completed the usual 2 years' hospital appointments and then gained experience in general practice by acting as locum tenens.

In 1936 he decided to specialize in radiology. He was first appointed as Medical Officer to the Radium Beam Therapy Research Unit at the Radium Institute, London, under Dr. Constance Wood, where cancer patients were being treated with two 5-gram radium bombs. From there he was appointed Registrar on the staff of the Meyerstein Institute of Radiotherapy at the Middlesex Hospital under Prof. Sir Brian Windeyer, in January 1937. He obtained the D.M.R.E., Cambridge, in June 1938. He was then appointed Senior Assistant Radiotherapist; a position he held until he returned to South Africa in June 1939.

In South Africa he joined the late Dr. F. H. Dommisse of Cape Town in private practice as a specialist in radiology and electro-therapeutics, and was appointed part-time radiologist to the South African Railways and Harbours Sick Fund (Cape Western Area), a post he held for 13 years until he left Cape Town for Pretoria.

In June 1952 he was appointed to the staff of the Department of Radiology at the Pretoria General Hospital and as senior lecturer in radiology at the University of Pretoria. During the next 5 years he obtained the degrees of M.Med. (Rad. T.) *cum laude* (in 1953); M.D. (in 1955); and D.Sc. (in 1957) at the University of Pretoria.

In 1957, when the Departments of Radiodiagnosis and Radiotherapy were completely separated, Prof. S. F. Oosthuizen remained Head of the Department of Radiodiagnosis, and Dr. Fichardt was appointed Head of the Department of Radiotherapy at the University of Pretoria and the Pretoria General Hospital. He has now been promoted to a full Professor of Radiotherapy. He is in charge of a modern department of radiotherapy where use is made of all types of ionizing radiations, including a 2,000-curie telecobalt unit for the treatment of cancer. There is a 32-bed ward, divided into 4- and 2-bed wardlets, which is directly under his supervision. During the past 18 months 2,545 new cancer cases were treated in the Department of Radiotherapy.

While in Cape Town, he was honorary secretary of the Cape Western Branch of the Medical Association for 4 years and President of the Cape Western Branch of the Society of Radiologists of South Africa for 1 year. Now in Pretoria, he is a member of the Medical/Biological Sub-committee of the Atomic Energy Board of South Africa, having been appointed in 1956. In 1958 he was elected a Fellow of the World Health Organization and awarded a grant to study the medical uses of atomic energy with special reference to super-voltage therapy, including telecobalt therapy at institutions overseas. After visiting radiotherapeutic institutions in Switzerland (there attending the Atoms for Peace Conference as an observer), France, the United Kingdom, Denmark, Sweden, and Germany, he returned to South Africa in December 1958. During the 28 years since he qualified he has published about 30 articles on subjects pertaining to radiotherapy and radiodiagnosis.

Professor Fichardt is married to Miss Etrechia Steytler, eldest daughter of Mrs. Eleonore Steytler, and the late Mr. Louw Steytler, M.P., of Burgersdorp, Cape Province.

IN DIE VERBYGAAN : PASSING EVENTS

Dr. A. H. Tonkin, Secretary of the Medical Association of South Africa, has been elected, after examination, as Associate Member of the Institute of Company Secretaries of South Africa.

Dr. A. H. Tonkin, Sekretaris van die Mediese Vereniging van Suid-Afrika is na aflegging van 'n eksamen toegelaat as Medelid van die Instituut van Maatskappy-sekretarisse van Suid-Afrika.

* * *

Members are reminded that they should notify any change of address to the Secretary of the Medical Association of South Africa at P.O. Box 643, Cape Town, as well as to the Registrar of the South African Medical and Dental Council, P.O. Box 205, Pretoria. Failure to advise the Association will result in non-delivery of the *Journal.* This applies to members proceeding overseas as well as those who change their addresses within the Union.

* * *

Dr. S. Klempman, of the Department of Pathology of the South African Institute for Medical Research, attended the Congress on Exfoliative Cytology in Vienna from 30 August - 2 September 1961. Before returning to South Africa, Dr. Klempman will visit Exfoliative Cytology Units in Paris, London, Newcastle and Oxford.

* * *

Dr. J. Kaufmann of the Neuropathology Department of the South African Institute for Medical Research, is attending the Congress on Neuropathology at Munich in September. Before returning to South Africa he will spend some time at neuropathological centres in London, Paris, Rome, Athens and Cairo, and will attend the Congress of Neurology in Rome.

* * *

Dr. W. Winterton, general practitioner of Perth, Western Australia, wishes to take over an assistant into his practice and requests that any South African doctor with British qualifications who may be interested should contact him. His address is 81 Scarborough Beach Road, Mt. Hawthorne, Perth.

* * *

Dr. C. Bam has commenced practice as an obstetrician and gynaecologist in Worcester. His address is Sanlam Buildings, Church Street, Worcester. Telephones: Rooms 4328, residence 4338.

Dr. C. Bam het begin praktiseer as verloskundige en vroue-arts in Worcester. Sy adres is Sanlam-gebou, Kerkstraat, Worcester. Telefone: Kamers 4328, woning 4338.

* * *

The Foundation 'Nicolò Castellino', of the National Institute for Insurance against Trade-accidents, is organizing a prize competition for the best original and unpublished work on the subject of Occupational Diseases Medicine; the choice of the topic will be left entirely to the candidates and the character of the work must be strictly scientific. The competition is open to all interested in the subject of occupational diseases medicine, who are neither university professors nor officially engaged in the teaching profession. Candidates must not be more than 40 years of age on 31 December 1962. Papers may be submitted in one of the following languages: Italian, French, German, English, Spanish, or Portuguese. Should any further information be required, the prospective participants may write directly to the Segreteria della Fondazione 'Nicolò Castellino', c/o INAIL, Via IV Novembre 144, Rome.

* * *

Dr. Rhoderic W. A. Nel, of Cape Town, wishes to inform his colleagues that he is not in partnership as had been announced, but that he is still in practice on his own as a gynaecologist and obstetrician at 403 Groote Kerk Buildings, Cape Town, as well as Bellville Medical Centre, Volkskas Buildings, Bellville.

Dr. Rhoderic W. A. Nel, van Kaapstad, wens hiermee sy kollegas in kennis te stel dat hy nie in vennootskap, soos aangemeld, is nie en dat hy nog alleen as ginekoloog en verloskundige by Groote Kerk-gebou 403, Kaapstad, sowel as Bellville Mediese Sentrum Volkskas-gebou, Bellville, praktiseer.

* * *

Dr. Ben Epstein, of Pretoria, who is the Vice-chairman of the World Commission on Cerebral Palsy, has returned to South Africa from Vienna, where he attended a Seminar on 'The evaluation of therapy in the cerebral palsied child', which was arranged by the Commission.

* * *

South African Institute for Medical Research, Johannesburg, Staff Scientific Meeting. The next meeting will be held on Monday 25 September 1961 at 5.10 p.m. in the Institute Lecture Theatre. Mr. A. K. Lorimer and Miss V. Brandt will talk on 'Microbiological assay of vitamins'.

* * *

Dr. W. H. Davis, of the Cardiac Unit, Pretoria Central Hospital, has been awarded a Lederle International Fellowship for Medical Research in the United States of America. Dr. Davis commences his studies at Tulane University, New Orleans, this month.

The Lederle International Fellowship is sponsored by the Cyanamid International Company, who every year provides fellowships for medical men from all over the world.

* * *

Christian Medical Fellowship. A sandwich lunch will be held on Wednesday 27 September at the Cafeteria in the Architecture Building, University of Cape Town, at 12.45 - 2.00 p.m. Dr. J. F. Jarvis will speak on 'Materialism'.

Christelike Geneesherebond. Toebroodjies en koffie sal bedien word op Woensdag 27 September om 12.45 - 2.00 nm. in die Kafeteria in die Argitektuur-gebou, Universiteit van Kaapstad. Die spreker is dr. J. F. Jarvis en sy onderwerp is ‚Materialisme'.

NUWE PREPARATE EN TOESTELLE : NEW PREPARATIONS AND APPLIANCES

SENOKOT

Reckitt & Colman (Africa) Limited announce that they have taken over the manufacture and distribution of Westminster Laboratories products, the most widely known of which is Senokot.

This first fully active and standardized preparation of senna is today the most widely prescribed stimulant laxative under the British National Health Scheme, and is in routine use in more than 6,000 hospitals in Britain and the United States.

The fact that there have been more than 90 references to

this preparation in recently published medical and technical literature indicates that it has become the laxative of choice in many fields, including paediatrics, geriatrics, obstetrics and gynaecology.

Although Senokot '(1) is both palatable and efficient . . . a valuable ally in the care of chronic constipation as well as an aperient for occasional use' . . . it is valued most highly for its re-educative effect on the constipated bowel. '(2) This standardized senna derivative, as predicted on experimental grounds, acts in a way almost indistinguishable from the normal physiological mechanism . . . it rehabilitates and re-educates the constipated bowel toward resumption of normal reflex activity . . . It is the most logical product to be used when intestinal tonus is impaired during pregnancy.'

Presentation. Senokot is available in pleasant-tasting chocolate-flavoured granules or in tasteless tablets. Chocolate-flavoured granules 2 oz. tins; 6 oz. tins; 2 lb. tins (Hospital Pack). Tablets. 50; 200, 1,000 (Hospital Pack).

Dosage. The correct dose is that which gives a comfortable formed motion. This dose is usually found within the following range although more or less may be required.

Adults: 1 - 2 teaspoonfuls granules or 2 - 4 tablets. In obstinate cases up to 2 teaspoonfuls or 4 tablets twice daily.

Children: One half of the adult dose.

Doses of more than 2 teaspoonfuls or 4 tablets are best divided and taken night and morning, or as prescribed by the physician.

Samples and further information may be obtained from Reckitt & Colman (Africa) Limited, (Pharma. Div.) P.O. Box 1097, Cape Town.

PRIPSEN

Reckitt & Colman (Africa) Limited announce the introduction of Pripsen, Westminster Laboratories single-dose treatment for both roundworms and threadworms.

In pleasant-tasting granule form, which may be eaten direct from a spoon, sprinkled on food or mixed with milk to form an agreeable drink, Pripsen contains piperazine phosphate and standardized senna (Senokot). 10 grammes of granules (a full dose) contains 4 grammes of piperazine phosphate B.P. and standardized Senna equivalent to 28 m.g. Sennosides A and B. The exceptional therapeutic efficiency of Pripsen has been reported by White and Scopes (1960) as follows:

Material and Methods

Enterobius vermicularis was confirmed by identification of ova on 'sellotape' swabs. Each child was given a single dose of Pripsen at bedtime, and thereafter 'sellotape' swabs were taken each morning for 10 days. The criterion of cure was 7 consecutive negative swabs.

Children aged 2 - 5 years received 7·5 gr. of Pripsen (=3 grammes piperazine phosphate) and children aged 6 - 12 years received 10 gr. (=4 grammes piperazine phosphate).

Results

1. Of 59 children treated 57 were cured. This represents a cure-rate of 97 per cent. 2. The rate of disappearance of ova, assessed by daily swabbing, was remarkably rapid. 3. The total dose of piperazine used in each case was less than half that hitherto used in a seven-day course. 4. Side-effects were negligible and toxic effects with a single dose are unlikely to occur. 5. Since a single dose can be given under supervision the risk of treatment not being completed has been eliminated.

Pripsen, therefore, has been shown to give, in a single dose, a cure rate for threadworms (pinworms) as high as that previously obtained with the usual seven-day treatment.

Dosage and Administration. 6 years and over, 10 gr., a full dose (contents of a single-dose tube of 4 teaspoonfuls). Under 6 years, half to three-quarters of the full dose.

Presentation. Tubes of 10 grammes (one full dose), tins of 450 grammes (45 full doses).

Samples and further information from Reckitt & Colman (Africa) Limited, (Pharma. Div.) P.O. Box 1097, Cape Town.

TENUATE DOSPAN

Mer-National Laboratories are pleased to announce the availability of Tenuate Dospan, a new presentation of Tenuate for 12-hour hunger control with a single daily dose, and supply the following information:

Because of the virtual absence of central-nervous-system stimulation, Tenuate is frequently selected as the anorectic of choice, especially for 'special risk' patients where obesity accompanies cardiac/hypertensive disease, diabetes, pregnancy, etc.

Tenuate is a safe anorectic of proved efficiency. Tenuate Dospan provides all these benefits in a new long-acting form — a single tablet in mid-morning provides hunger control for a full 12 hours. It is based on a unique principle in long-acting medication which meets each of the three desirable criteria: continuous release, uniform release, and predictable effect. The Dospan principle is continuous release from a colloid carrier triggered by moisture alone.

The active principle is intimately blended with a special hydrophilic colloid which absorbs moisture to form a jelly-like water barrier at the surface of the tablet, which expands slightly. Peristalsis dislodges surface colloid particles and small amounts of drug — the water barrier reforms and the process is continually repeated over an 8 - 10 hour period. A relatively constant surface area is maintained throughout, ensuring a uniform rate of drug release. This process is independent of the pH of gastric contents.

Presentation. Tenuate Dospan is available in bottles of 30 tablets. Each tablet contains 75 mg. of diethylpropion in continuous-release dosage form.

A PAEDIATRIC SYRUP FORM OF HUMATIN

Parke, Davis have introduced Humatin Syrup (paramomycin, Parke, Davis) a pleasant root-beer flavoured liquid form of their new antibiotic Humatin, which has both broad-spectrum antibacterial and amoebicidal properties.

Indications: Humatin Syrup is ideally suited for the treatment of paediatric patients with bacillary dysenteries and diarrhoeas caused by salmonella, shigella, and *Esch. coli* organisms as well as the management of undiagnosed non-specific infections.

It is unusually effective in clearing all phases of intestinal amoebiasis — sub-acute, acute and chronic.

Humatin Syrup is also beneficial in preoperative suppression of the intestinal flora prior to bowel surgery and as adjunctive therapy in the management of hepatic coma.

Dosage and Administration:

1. *Bacillary dysenteries:* 35 - 100 mg. per kg. of bodyweight in divided doses daily for six days.
2. *Intestinal amoebiasis:* 25 - 100 mg. per kg. of bodyweight in divided doses at mealtimes daily for at least five days.
3. *Prior to bowel surgery:* a dose of 500 mg. four times daily for four consecutive days.
4. *Management of hepatic coma:* amounts of Humatin up to 6 G. per day in divided doses have produced good results.

Package Information: Humatin Syrup is available in 60 ml. bottles, containing the equivalent of 125 mg. paromomycin base per 5 ml.

Further information is obtainable from Parke, Davis Laboratories (Pty.) Ltd., P.O. Box 24, Isando, Transvaal.

BOEKBESPREKINGS : BOOK REVIEWS

MANAGEMENT OF THE PATIENT WITH BRAIN DAMAGE

Evaluation and Management of the Brain-Damaged Patient. By Jerome S. Tobis, M.D., and Milton Lowenthal, M.D. Pp. xii + 109. 33 illustrations. R4.80. Oxford: Blackwell Scientific Publications and Springfield, Illinois: Charles C. Thomas. 1960.

This book fills a gap which has long existed in the management of the brain-damaged patient. The magnitude of the problem relating to brain-damaged patients becomes startlingly evident when it is realized that 1·8 million persons in the USA are today suffering from hemiplegia; that there are 500,000 children suffering from cerebral palsy; and that some 800,000 persons are suffering from epilepsy. This does not take into account mental retardation from whatever cause.

The brain-damaged patient is classified within the framework of infections, intoxication, trauma, circulatory disturbances, convulsive disorders, metabolic disturbances, and primary and secondary neoplasms.

Since human behaviour depends on a synthesis of the activity of the musculo-skeletal, visceral and nervous systems, evaluation is based upon the interpretation of sensory, motor and psychological function. Psychological functions include disturbances of emotional response.

The management and rehabilitation of the brain-damaged patient follows along well-defined and topically accepted patterns. Of particular interest is the evaluation and treatment of the cerebral palsied child, and the rehabilitative measures used in the treatment of the paraplegic. Bracing and crutches are discussed all too briefly.

The book is well illustrated and well printed, and can be thoroughly recommended to the medical man whose interest lies in the field of locomotor disorders. C.W.C.

NEURO-OPHTHALMOLOGY

Clinical Methods of Neuro-Ophthalmologic Examination. Second completely revised and enlarged edition. By Alfred Kestenbaum, M.D. Pp. xii + 577. Illustrated. $16.75. New York and London: Grune and Stratton. 1961.

The publication of a second edition of this work only fifteen years after the first, is an indication of its popularity. Both for the ophthalmologist and neurologist this work is of vital importance, bringing as it does the gap between these two specialties.

This edition remains essentially clinical with a detailed exposition of all ocular tests relating to neuro-ophthalmology, placing some emphasis on those attributed to the author. The chapter on visual fields and their interpretation is excellent. Specialized investigations such as the E.R.G. and pupillometry, have been added, but wisely confined to their clinical application.

It is natural that many of the author's expressed views should be controversial. However, positive exception must be taken to at least two statements, the one that retrobulbar neuritis occurs frequently in diabetes (p. 140), and the other that the physiological cup may reach the inferior or temporal margin of the disc (p. 269).

This work has its faults, but on the whole it serves as a most valuable reference to a difficult subject. M.H.L.

MEDICAL TREATMENT

Textbook of Medical Treatment. By various authors. Edited by Sir Derrick Dunlop, B.A. (Oxon.), M.D., F.R.C.P. Ed., F.R.C.P. Lond., Sir Stanley Davidson, B.A., M.D., Hon. M.D. (Oslo), F.R.C.P.Ed., F.R.C.P. Lond., and S. Alstead, C.B.E., M.D., F.R.C.P.Ed., F.R.C.P. Lond., F.R.F.P.S. Pp. xix + 983. R6.00. 33c postage. London: E. & S. Livingstone. 1961.

When the first edition of this book appeared in 1939, it was stated that the authors had attempted to be 'extremely explicit in regard to treatment recommended'. Alhough it has now reached its eighth edition, with an additional seven reprintings, it has kept to this standard and one has the knowledge that methods of treatment contained in it are founded on wide experience.

It is not a 'picture book', for there are indeed few illustrations. It is a textbook, and all the pictures of cases one needs are contained in the text. A.H.T.

BRIEWERUBRIEK : CORRESPONDENCE

DIFFERENTIAL SALARY SCALE

To the Editor: While we are awaiting the result of the Federal Council's deliberations, it may be of interest to know that when I raised the matter of differential salary scales at this hospital some weeks ago I was told that it had been taken as far as we can go, i.e. to the Minister of Health, and until he acts no progress will be made. Here is the root of the problem. It is obviously a clash of policy and principle. The Government cannot create a precedent in salaries, even though it involves the medical profession.

This sort of stand may be excusable in that there are alternatives (private practice), but since the majority of our non-European population has, perforce, to accept hospital treatment, and since even the lure of higher salaries is not staffing our non-European hospitals with European doctors, it means that the State is failing in its responsibility for the bodily welfare of its inhabitants.

Non-European colleagues tell me that they would gladly stay in hospital service at a reasonable salary. I am sure no sane European would accept these conditions when private practice offers so much, so how can we ask the non-Europeans to accept them?

Ian Kennedy

King Edward VIII Hospital
Durban
25 August 1961

BELANGRIK — MEDIESE KONGRES

Registrasie op Sondag, 24 September 1961 in die Studente-Unie by die Universiteit van Kaapstad, sal vanaf 2 - 5 nm. plaasvind, en nie vanaf 10 vm. soos in die finale omsendbrief aangekondig is nie. Registrasie op Maandag, 25 September, begin om 8.30 vm. soos aangekondig.

IMPORTANT — MEDICAL CONGRESS

Registration on Sunday, 24 September 1961 in the Students' Union at the University of Cape Town, will take place from 2 - 5 p.m. and not from 10 a.m. as announced in the final circular. Registration on Monday, 25 September, commences at 8.30 a.m. as announced.